Université de Montréal

Aerobic Oxidations Catalyzed by Combinations of Transition Metal Salts and N-hydroxyphthalimide

par
Yi Jing Zhong

Département de chimie
Faculté des arts et des sciences

Mémoire présenté à la Faculté des études supérieures
en vue de l'obtention du grade de Maître ès Sciences (M. Sc.)
en chimie

Août, 2007

Université de Montréal
Faculté des études supérieures

Ce mémoire intitulé :

Aerobic Oxidations Catalyzed by Combinations of Transition Metal Salts and N-hydroxyphthalimide

présenté par :

Yi Jing Zhong

a été évalué par un jury composé des personnes suivantes :

.....

Christian Reber : président-rapporteur

.....

Davit Zargarian : directeur de recherche

.....

André L. Beauchamp : membre du jury

Résumé

Cette thèse décrit l'étude de réactions d'oxydation catalytiques aérobiques pour une grande variété de substances organiques avec l'objectif de développer un protocole général pour la bénéficiation de la bauxite. Nous avons établi que la combinaison de NHPI (N-hydroxyphthalimide) et de $Co(OAc)_2$ permet l'oxydation de plusieurs substrats à l'air ou sous atmosphère d'oxygène à des températures variant entre 20 et 80°C. Nos études ont aussi démontré que l'efficacité catalytique était assez constante, que NHPI ou son dérivé 4-nitro-NHPI soit utilisé.

La plupart de ces études catalytiques ont été menées dans des solvants organiques tels que l'acétate d'éthyle ou l'acétonitrile, mais les réactions d'oxydation peuvent aussi bien être menées en milieu aqueux, quoique avec une efficacité moindre. Un aspect intéressant est qu'avec l'usage d'une importante quantité de catalyseur à base de fer combiné au NHPI, l'efficacité de l'oxydation peut atteindre celle du système $Co(OAc)_2$/NHPI. Dans quelques cas, la présence de catalyseurs de transfert de phase a amélioré de façon importante l'efficacité de l'oxydation aqueuse pour les réactions impliquant $Co(OAc)_2$. Les catalyseurs de transfert de phase n'ont pas offert autant de bénéfice pour les oxydations aqueuses impliquant les sels de fer. Par exemple, les oxydations faisant usage de $Fe(NO_3)_3$ et de NHPI se produisaient assez bien dans de l'eau ne contenant pas de catalyseur de transfert de phase.

Nous avons aussi étudié l'oxydation de matières organiques présentes dans des échantillons de bauxite. De façon significative, l'utilisation de seulement NHPI

sans ajout de sels métalliques donnait lieu à de l'oxydation en milieux aqueux basique, ce qui implique peut-être que des sels métalliques présents dans la bauxite (ex : Fe_2O_3) soient extraits dans le milieu réactionnel. Nous avons étudié les spectres UV-Visible de solutions de $Co(OAc)_2$/NHPI pour tenter d'identifier les espèces actives dans ce système catalytique.

Mots-clés : oxydations aérobiques catalytiques, bauxite, NHPI, 4-nitro-NHPI, $Co(OAc)_2$, $Fe(NO_3)_3 \cdot 9H_2O$, Fe_2O_3

Abstract

This thesis describes studies on catalytic aerobic oxidation reactions of a wide range of organic substances with the objective of developing a general protocol for bauxite beneficiation. We have found that the combination of NHPI (N-hydroxyphthalimide) and $Co(OAc)_2$ promotes the oxidation of many substrates in air or pure oxygen at temperatures varying between 20 and 80 °C. Our studies also showed that the catalytic efficiency was fairly constant whether we used NHPI or its derivative 4-nitro-NHPI.

Most of the catalytic studies were carried out in organic solvents such as ethyl acetate or acetonitrile, but oxidation reactions can also proceed in aqueous media, albeit with lower efficiencies. Interestingly, with the use of a large amount of iron-based catalysts combined with NHPI, the oxidation efficiencies could reach those of the system of $Co(OAc)_2$/NHPI. In some cases, the presence of phase transfer catalysts improved greatly the aqueous oxidation efficiency for the $Co(OAc)_2$ reactions. On the other hand, phase transfer catalysts did not offer as much benefit for aqueous oxidations using iron salts. For instance, oxidations using $Fe(NO_3)_3$ and NHPI proceeded fairly well in water not containing phase transfer catalysts.

We have also studied the oxidation of organic matter present in bauxite samples. Significantly, using only NHPI without added metal salts allowed some oxidation in basic aqueous media, implying perhaps that metal salts present in bauxite (e.g., Fe_2O_3) are extracted into the reaction medium. We have studied the UV-

visible spectra of $Co(OAc)_2$/NHPI solutions in an attempt to identify the active species in this catalytic system.

Keywords: Catalytic aerobic oxidations, bauxite, NHPI, 4-nitro-NHPI, $Co(OAc)_2$, $Fe(NO_3)_3 \cdot 9H_2O$, Fe_2O_3

Table of Contents

Chapter 1 : INTRODUCTION 1

1.1 Complication in purification of bauxite 3

1.2 Organic content of bauxite 7

1.3 Catalytic aerobic oxidations: a literature review 10
1.3.1 Different categories of oxidations 15
1.3.2 Literature review of metal-catalyzed oxidation protocols 16
1.3.2.1 Copper catalysts 17
Cleavage of carbon-carbon double bonds 17
Oxidation of alkanes and benzylic compounds 18
Oxidation of alcohol 20
1.3.2.2 Iron catalysts 21
Oxidation of alkanes 21
Oxidation of benzylic compounds 27
1.3.2.3 Manganese catalysts 28
1.3.2.4 Cobalt catalysts 29
Oxidation of alkanes 29
Oxidation of alkenes 30
Oxidation of benzylic compounds 31
1.3.2.5 Catalytic oxidation by NHPI 32
Principle of catalytic aerobic oxidation by NHPI 32
Combination of transition metal salts and NHPI for catalytic aerobic oxidations 34
N-Hydroxy phthalimide derivatives and analogues 37
Applications of catalytic oxidations by NHPI 40
Conclusions on the oxidation reactions promoted by NHPI 46

1.4 SCOPE OF THE JOINT UdeM-ALCAN PROJECT 47

Chapter 2 : EXPERIMENTAL SECTION 50

2.1 General 50

2.2 Procedures for oxidation reactions and for the preparations of the derivatives and analogues of NHPI 53

Chapter 3: AEROBIC OXIDATIONS CATALYZED BY COMBINATIONS OF NHPI OR 4-NITRO-NHPI, AND TRANSITION METAL SALTS 60

3.1 Aerobic oxidations catalyzed by $Co(OAc)_2$/NHPI 61
3.1.1 Aerobic oxidation in organic solvents 61
3.1.1.1 Oxidation of benzyl alcohol 61
3.1.1.2 Oxidation of styrene 62
3.1.1.3 Oxidation of toluene 68
3.1.1.4 Oxidation of cumene 68
3.1.1.5 Oxidation of indane 70
3.1.1.6 Oxidation of indene 70
3.1.1.7 Oxidation of *p*-xylene 76
3.1.1.8 Oxidation of fluorene 76
3.1.1.9 Oxidation of xanthene 77
3.1.1.10 Oxidation of isochroman 78
3.1.1.11 Oxidation of 2-phenyl-2-propanol, *trans*-cinnamic acid, and chromone 79
3.1.1.12 Oxidation of benzyl amine 79
3.1.1.13 Conclusions on oxidative reactions by $Co(OAc)_2$/NHPI in organic solvents 80
3.1.2 Oxidation reactions in aqueous media 81
3.1.2.1 Oxidation of benzyl alcohol 82
3.1.2.2 Oxidation of indene 83
3.1.2.3 Oxidation of isochroman 85
3.1.2.4 Oxidation of fluorene 87
3.1.2.5 Oxidation of indane 87
3.1.2.6 Oxidation of xanthene 88
3.1.2.7 Oxidation of *p*-xylene 89
3.1.2.8 Conclusion on oxidations of substrates in aqueous media 89

3.2 Aerobic oxidations catalyzed by iron catalysts/NHPI 90
3.2.1 Aerobic oxidations in ethyl acetate 90
3.2.2 Aerobic oxidations in aqueous media 93

3.3 Aerobic oxidations catalyzed by transition metal / 4-nitro-NHPI 97
3.3.1 Aerobic oxidation by $Co(OAc)_2$ / 4-nitro-NHPI in EtOAc 98
3.3.2 Aerobic oxidation catalyzed by $Fe(NO_3)_3 \cdot 9H_2O$/4-nitro-NHPI in aqueous media 99
3.3.2.1 Oxidation of benzyl alcohol 99
3.3.2.2 Oxidation of indane 100
3.3.2.3 Oxidation of isochroman 100
3.3.2.4 Oxidation of xanthene 101
3.3.2.5 Comparison of aqueous oxidations by $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI or 4-nitro-NHPI 102

Chapter 4: Aerobic Oxidations of Humic Acids and Bauxite 103

4.1 NHPI and $Co(OAc)_2$: UV-vis spectroscopy and thermal stability in aqueous media 103

4.2 Aerobic oxidations of humic acids 107

4.3 Aerobic oxidations of bauxite 110
4.3.1 Bauxite properties 111
4.3.2 Bauxite oxidation by NHPI with or without $Co(OAc)_2$ 114
4.3.2.1 Bauxite oxidation catalyzed by $Co(OAc)_2$/NHPI 114
4.3.2.2 Bauxite oxidation by NHPI without cobalt acetate 116
4.3.2.3 Bauxite oxidation by $Co(OAc)_2$ / NHPI 118
4.3.3 Conclusions on bauxite oxidations 119

Chapter 5: GLOBAL CONCLUSIONS 120

REFERENCES 123

List of Figures

Figure 1: Structures of some building blocks of humic substances (HSs) 9
Figure 2: The proposed structure of a humic acid, adapted from Schulten and Schnitzer 9
Figure 3: Catalytic oxidations of hydrocarbons.....11
Figure 4: Formation of nitriles by ammoxidation of alkenes, methyl aromatic and heteroaromatic compounds.....14
Figure 5: Transition state for the reaction of PINO with substituted benzenes.....39
Figure 6: The structures of 4-nitro-NHPI, 4-nitrophthalimide, and 4-nitrophthalic anhydride 55
Figure 7: GC spectrum of styrene oxidation for Run 2-3 67
Figure 8: MS spectrum of the unknown product at RT=15.67 min of styrene oxidation (Run 2-3) 67
Figure 9: GC spectrum of indene oxidation 71
Figure 10: Some MS spectra of oxidized products of indene oxidation 73-75
Figure 11: MS spectrum of the oxidized product **28** of xanthene oxidation 78
Figure 12: Comparison of aerobic oxidations catatlyzed by NHPI combined with cobalt acetate (0.5%) or ferric nitrate (5%) 93
Figure 13: Comparison of aqueous oxidations catalyzed by NHPI combined with cobalt acetate (2%) or iron catalysts (10%).....97
Figure 14: Comparison of oxidations in EtOAc catalyzed by cobalt acetate combined with 4-nitro-NHPI or NHPI 99
Figure 15: Comparison of aqeuous oxidation catalyzed by ferric nitrate combined with NHPI or 4-nitro-NHPI.....102
Figure 16: UV-vis spectrum of NHPI dissolved in water.....104
Figure 17: UV-vis spectra of NHPI, cobalt acetate, and the mixture of cobalt acetate and NHPI 105
Figure 18: UV-vis spectrum of aqueous NHPI solutions at various conditions..106

Figure 19: UV-vis spectra of new complexes of cobalt acetate and NHPI at RT and 80 °C 106
Figure 20: UV-vis spectrum of NHPI, phthalimide, phthalic anhydride, the decomposed product of NHPI 107
Figure 21: UV-vis spectrum of humic acid sodium salt solutions at different concentration 109
Figure 22: UV-vis spectrum of Aerobic oxidation of humic acid sodium salts catalyzed by cobalt acetate/NHPI 109
Figure 23: UV-vis comparison of oxidations of humic acid sodium salts catalyzed by cobalt aceate/NHPI in water or 0.001N NaOH 110
Figure 24: UV-vis spectra of bauxite in various aqueous conditions after 20-hour stirring at RT in air without catalysts 112
Figure 25: UV-vis spectrum of bauxite stirring in 0.001N NaOH in air (20-fold dilution, 1-, 10-, and 20 h samplings) 112
Figure 26: UV-vis spectrum of bauxite in 0.003N NaOH at different conditions without catalysts 113
Figure 27: UV-vis spectrum of bauxite in 0.001N NaOH with benzalkonium chloride (sampling at different time) 113
Figure 28: Comparison of UV-vis spectra of bauxite oxidations catalyzed by cobalt acetate/NHPI 115
Figure 29: UV-vis spectrum of bauxite oxidation catalyzed by $Co(OAc)_2$ / NHPI with or without pretreatment 116
Figure 30: Comparison of UV-vis spectra between at the beginning and at the end of bauxite oxidations catalyzed by NHPI alone 117
Figure 31: Comparison of UV-vis spectrum of bauxite oxidations catalyzed by NHPI 117
Figure 32: Comparison of UV-vis spectrum of bauxite oxidations catalyzed by NHPI with and without pretreatment 118
Figure 33: Comparison of UV-vis spectra of aerobic oxidations of pretreated bauxite catalyzed by NHPI or cobalt acetate/NHPI 119

List of Tables

Table 1: The model substrates representing the chemical diversity of HSs 10
Table 2: Oxidative cleavage of C=C bonds in aromatic vinyl ethers 18
Table 3: Aerobic Cu-catalyzed oxidations of alkanes in the presence of 18-crown-6 and acetaldehyde 20
Table 4: Aerobic iron-catalyzed oxidation reactions 23
Table 5: Aerobic oxidations of alkanes catalyzed by the Mn-porphyrin complex Mn(TPRPP)Cl in the presence of acetaldehyde 29
Table 6: Oxidations of 1,2-octanediol with O_2 35
Table 7: The effect of metal salts on aerobic oxidations of 3-methylpyridine catalyzed by NHPI 36
Table 8: The effect of $Mn(OAc)_2$ on aerobic oxidations of 3-methylpyridine by $Co(OAc)_2$/NHPI 36
Table 9: Aerobic oxidations of secondary alcohols by $Co(OAc)_2$/NHPI/O_2 41
Table 10: Aerobic oxidations of diols by $Co(acac)_3$/NHPI/O_2 42
Table 11: Aerobic oxidations of alkylbenzenes by $Co(OAc)_2$ (0.5 mol%) / NHPI (10 mol) / O_2 (1 atm) at 25 °C 43
Table 12: Aerobic oxidations of benzylic compounds (1 mmol) by NHPI (0.1 mml) and acetaldehyde (1 mmol) at room temperature 45
Table 13: List of chemicals used 51-52
Table 14: GC/MS conditions 53
Table 15: Aerobic oxidations of various substrates in organic solvents catalyzed by $Co(OAc)_2$ / NHPI in air or under 1 atm of O_2 63-65
Table 16: Peaks in GC spectrum of styrene oxidation for Run 2-3 (Figure 7) 66
Table 17: Peaks in GC spectrum of indene oxidation (Figure 9) 72
Table 18: Benzyl alcohol oxidations by $Co(OAc)_2$ / NHPI in aqueous media 83
Table 19: Indene oxidation catalyzed by $Co(OAc)_2$ / NHPI in aqueous media 84
Table 20: Isochroman oxidations by $Co(OAc)_2$ / NHPI in aqueous mixtures 85

Table 21: Isochroman oxidations catalyzed by $Co(OAc)_2$/NHPI in water with or without surfactants 85
Table 22: Isochroman oxidations catalyzed by $Co(OAc)_2$/NHPI with various concentration of surfactant 86
Table 23: Comparison of isochroman oxidation catalyzed by $Co(OAc)_2$ / NHPI in various basic aqueous media 86
Table 24: Oxidations of fluorene by $Co(OAc)_2$ / NHPI in aqueous media 87
Table 25: Indane oxidations catalyzed by $Co(OAc)_2$ / NHPI in aqueous media ... 88
Table 26: Xanthene oxidations by $Co(OAc)_2$ / NHPI in aqueous media 88
Table 27: *p*-Xylene oxidations in aqueous media by $Co(OAc)_2$ / NHPI 89
Table 28: Selection of proper ironic catalysts from oxidations of isochroman 91
Table 29: Comparison of oxidative efficiencies catalyzed by various iron salts combined with NHPI 92
Table 30: Comparison of catalytic oxidations of indane by NHPI in various aqueous solutions combined with iron salts or cobalt acetate 94
Table 31: Comparison of isochroman oxidations in various aqueous solutions catalyzed by NHPI combined with cobalt acetate or iron salts 95
Table 32: Comparison of xanthene oxidations in various aqueous solutions catalyzed by NHPI combined with cobalt acetate or iron salts 95
Table 33: Comparison of aerobic oxidations in EtOAc catalyzed by $Co(OAc)_2$ combined with 4-nitro-NHPI or NHPI 98
Table 34: Aerobic oxidation of indane catalyzed by $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI or 4-nitro-NHPI in aqueous media 100
Table 35: Aerobic oxidation of isochroman by $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI or 4-nitro-NHPI in aqueous media 101
Table 36: Aerobic oxidation of xanthene by $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI or 4-nitro-NHPI in aqueous media 101

List of Abbreviations

BDEs: bond dissociation energies

DBAD: di-*tert*-butyl azodicarboxylate

DMAP: dimethylaminopyridine

EPR technique: Electron Paramagnetic Resonance technique

EtOAc: ethyl acetate

FAs: Fulvic acids

GC/MS: Gas Chromatography/Mass Spectrometry

HAs: Humic acids

HSs: Humic substrates

*i*Pr: isopropyl

MCBA: *m*-chlorobenzoic acid

MMO: monooxygenase

mmol: millimole

NAPI: N-acetoxyphthalimide

NHPI: N-hydroxyphthalimide

4-nitro-NHPI: 4-nitro-N-hydroxyphthalimide

NMR: Nuclear magnetic resonance

Phen: phenanthroline

PINO radical : phthalimide N-oxyl radical

PolyDADMAC: Polydiallyldimethylammonium chloride

SMDT: [3-(salicylidiemeimino)propyl]methylaminato

tert: tertiary

t-Bu: *tert*-butyl

TBHP: *t*-BuOOH

THF: tetrahydrofuran

THICA: N, N', N"-Trihydroxyisocyanuric acid

TON: Turnover number, mmols of products per mmol of the catalyst used

Acknowledgement

I would like to express my gratitude to all those who enabled me to complete this thesis.

First of all, I would sincerely like to thank Alcan Inc. for sponsoring this project. I am also deeply grateful to Dr. Sebastien Fortin, who supervises the project at Alcan, for his help and advice.

I would like to express my deep and sincere gratitude to my supervisor, Prof. Davit Zargarian, who gave me the opportunity to work on this project. His broad knowledge and his logical way of thinking have been of great value for me. His understanding, encouraging, and guidance have provided a good basis for the present thesis. Without his help, this dissertation would not have been possible.

I deeply thank Annie Castonguay, Christine Sui-seng, and Nathalie Baho, who taught me how to work in the lab, how to use various techniques, for example, NMR, UV-vis and IR, and gave me a lot of useful suggestions about work. Without them I cannot finish my experiments successfully. In addition, I also thank Valerica Pandarus and Jason Vachon for their help. I am also grateful to these individuals for their friendships.

Finally, I would like to give my special thanks to my husband Jun Qi and my daughter Ruo Ying Qi. They have lost a lot due to my absence from home. Without their encouragement and understanding it would have been impossible for me to finish this work. Special thanks are also due to my parents and my sister for their loving support.

Chapter 1 : INTRODUCTION

Aluminum and aluminum alloys are used extensively in industrial or domestic applications where a strong, light, easily constructed material is needed, for example, the construction of cars, buses, trains, and aircrafts. Generally, the production of aluminum is based on bauxite, the most important aluminum-containing ore. Bauxite consists largely of the Al minerals gibbsite, $Al(OH)_3$, boehmite and diaspore, AlO(OH), together with the iron oxides goethite, FeO(OH), and hematite, Fe_2O_3, the clay mineral kaolinite ($Al_2O_3 \cdot 2SiO_2 \cdot 2H_2O$) and small amounts of titanium oxides (TiO_2). Bauxite is typically 40-50% alumina (Al_2O_3) in weight. According to the British Geological Survey, Australia was the top producer of bauxite in 2005, with almost one-third world share; other major producers of bauxite are Brazil, China and Guinea. The production of aluminum is based on two processes, the Bayer process and the Hall-Héroult process, which are described briefly below.

The Bayer process. This process contains three main stages: extraction, precipitation, and calcination. During extraction, the aluminum-bearing minerals (gibbsite, boehmite, and diaspore) are selectively extracted from the insoluble components (iron oxides and other impurities) by dissolving them in pressure vessels with a hot concentrated caustic soda solution (ca. 5M NaOH) for a few minutes. The temperature and duration of this first stage of this treatment – also called "digestion" – depend on alumina species contained in the bauxite (Eq. 1 and 2). Generally, the ore is crushed and milled to make the minerals more available for

extraction. Moreover, hot sodium hydroxide is added to the bauxite at ~90 °C to dessilicate prior to digestion. This stage is required to convert kaolinite into sodalite, an insoluble sodium alumino-silicate (Eq. 3). After digestion, the red mud, which consists of the insoluble bauxite residue, mainly including Fe_2O_3, TiO_2, and sodalite, must be separated from the aluminum-containing mother liquor by a decantation process. The mother liquor is purified through filters before being transferred to the precipitators, and the red mud is thickened and washed to recover the caustic soda, which is then recycled back into the process. Flocculants (polyacrylamides, polyacrylates) are added to accelerate the decantation.

$$Al(OH)_3 \text{ (gibbsite)} + NaOH \rightarrow Na[Al(OH)_4] \qquad 140\text{-}150\ ^\circ C \qquad \text{(Eq. 1)}$$

$$AlO(OH) \text{ (boehmite)} + NaOH + H_2O \rightarrow Na[Al(OH)_4] \qquad 220\text{-}250\ ^\circ C \qquad \text{(Eq. 2)}$$

$$2[Al_2O_3 \cdot 2SiO_2 \cdot 2H_2O] + 6NaOH + Na_2CO_3 \rightarrow$$

$$2[Na_2O \cdot Al_2O_3 \cdot 2SiO_2 \cdot 2H_2O] \cdot Na_2CO_3 + H_2O \qquad \text{(Eq. 3)}$$

In the precipiation stage, the pregnant liquor is cooled down to 60-80 °C, and crystalline aluminum trihydroxide (gibbsite), conventionally called "hydrate", is then precipitated in the presence of seed crystals (Eq. 4). The "hydrate" crystals are then classified into size fractions and the coarser product is sent to calcination. Undersized particles are recycled in the precipitation stage to serve as seeds. The remaining liquor, named spent liquor, which contains caustic soda and some alumina, goes back to the digesters.

$$Na[Al(OH)_4] \rightarrow Al(OH)_3 + NaOH \qquad \text{(Eq. 4)}$$

Finally, the hydrate is washed to remove any remaining caustic, and then heated to about 1050 °C in a rotary kiln or fluidised bed calciner to drive off the water and form alumina (Eq. 5).

$$2\ Al(OH)_3 \rightarrow Al_2O_3 + 3\ H_2O \qquad \text{(Eq. 5)}$$

The Hall-Héroult process. The pure alumina obtained from the Bayer process is melted at approximately 1000 °C in a carbon-lined bath of molten cryolite (Na_3AlF_6), which is used as a flux, and reduced to metallic aluminum by a highly energy-consuming electrolytic process. Meanwhile, aluminum fluoride (AlF_3) is used to reduce the melting point of the cryolite. The liquid aluminum is deposited at the cathode, while the carbon anode is oxidized and bubbled away as carbon dioxide (Eq. 6).

$$2\ Al_2O_3 + 3\ C \rightarrow 4\ Al + 3\ CO_2 \qquad \text{(Eq. 6)}$$

1.1 Complication in purification of bauxite

Most bauxites contain about 0.1 - 0.2% organic carbon, but low-quality (surface) bauxite occasionally contains up to 0.5% organic carbon.[1] This organic carbon, which is often present in the form of humic substances, gets extracted into the Bayer liquor as sodium salts of the degradation products (e.g., sodium oxalate) during the digestion stage.[1,2] Even though the relative proportion of organics is small, the large amount of bauxite that has to be treated in a closed-loop circuit (Bayer process) rapidly increases the concentration of organics in the liquor to the

levels that are detrimental to the process. In several plants, this problem is a major limitation on productivity. The contamination of Bayer liquor from organics causes many problems.

The complex mixture of organic compounds formed and degraded during digestion of bauxite and liquor recirculation also significantly contributes to caustic (NaOH) consumption. The increase in ionic strength due to organic soda formation can limit caustic concentrations manageable in refinery liquor and thereby refinery productivity. Some of these organic species also have a significant impact on the rate of gibbsite precipitation.

Overall, organic compounds can give rise to a number of process problems namely:

1) Lower alumina yield;
2) Generation of excessive amount of fine hydrate particles;
3) Higher impurity content in calcined alumina (sodium oxide);
4) Deactivation of seeds;
5) Loss of caustic due to the formation of sodium organic compounds;
6) Low settling rate in decanters;
7) Additional ballast to be heated and pumped continuously, etc.

Many potential solutions have been explored for removing humic matter from bauxite, or reducing their negative effects in the Bayer process. For example, the bauxite is roasted, the liquor is burnt, additives such as polyDADMAC have been used (these are water or waste water treatment cationic coagulators), and floatation/leaching/separation techniques have been applied to remove sulfide and carbonate fractions. These interventions result in significant additional costs to the

whole process and increase its degree of complexity while producing marginal improvements only to the quality of the treated liquor.

With the rapid depletion of high-quality bauxite, the aluminum industry is using more and more low-quality bauxite, so that the adverse effects of the organic impurities in the production of aluminum become more important.

Two strategies can be considered to control the organics in the Bayer process: destruction of the organics in the Bayer liquor, or their removal from the bauxite ore prior to its introduction in the plant. The former involves the treatment of significant amounts of liquor supersaturated with regards to alumina and silica, which means potential operational problems. The latter strategy, referred to as "bauxite beneficiation", is the preferred approach.

A simple and safe beneficiation process aimed at the removal of organics from bauxite would be a heap leaching step where the humic organic molecules are catalytically oxidized in order to render them more soluble in water. The aqueous leaching solution (water as is, or slightly alkaline water), containing the catalytic oxidizing system, would be used to solubilize the bauxite organic content. The leachate would be removed from beneficiated bauxite by a simple filtration or decantation process prior to the bauxite introduction into the plant. Due to the huge amounts of bauxite ore to be treated, a catalytic approach is a must in order to avoid the use of large quantities of oxidants.

A project undertaken by the Prof. Davit Zargarian group in collaboration with Dr. Sébastien Fortin of the Alcan Arvida Research and Development Centre explores the feasibility of using catalytic aerobic oxidation reactions to degrade the

organic matter present in bauxites in order to facilitate its removal prior to processing the bauxite. Our main strategy is to use highly effective oxidizing reagents to break up the macromolecular structure of the humic substances present in bauxites, thereby altering their amorphous nature and rendering them more soluble in mildly caustic solutions. This problem has been studied since February 2005 by using simple organic molecules as model substrates for developing a catalytic oxidation system. At this initial stage, our main pre-occupation is to devise a protocol for laboratory-scale oxidation of organic compounds and explore various ways of optimizing the reaction conditions to allow practical large-scale tests on humic acid or bauxite samples. Some of the major issues facing us at the outset were the simplicity of the experimental procedures and the choice of quantitative methods for measuring the effectiveness of the oxidation process.

This chapter includes three main sections: organic content of bauxite, literature review, and scope of this project. The first section of this report will give an overview of what is known about the organic content of bauxite, plus a brief description of the structure of humic substances and the various categories of substances identified therein. This section will serve as a base for identifying target compounds for the oxidation process and will help define our approach. The second section deals with metal-catalyzed oxidation protocols. Given that catalytic aerobic oxidation is, to our knowledge, a relatively new area of investigation in the context of aluminum production,[3] it was deemed appropriate to supplement the first account of our results with a literature review on the most promising catalytic oxidation systems. This section has allowed us to analyze the various oxidation strategies in terms of simplicity, relative expense of the oxidant, the reaction conditions,

and several other factors. The last section will explain the specific object of my project and provide the scope of our studies.

1.2 Organic content of bauxite

A good knowledge of the chemistry and properties of organic compounds present in bauxite is critical for developing ways to remove them altogether or reduce their content. As mentioned above, the organic matter present in bauxite is believed to be mainly in the form of humic substances, which originate from a mixture of plant and animal products in various stages of decomposition. In an internal report prepared for Alcan, K. The has raised the possibility that bauxites contain other sources of organic matter such as carbohydrates, polysaccharides, and even low molecular weight compounds such as citric and oxalic acids.[2] In addition, this report states that the definition of humic substances in the alumina industry is ambiguous, most discussion of this subject referring to "the organic species responsible for the dark colouration of Bayer process liquor", or "the high molecular weight organic fractions arising from the degradation of bauxite organics upon digestion". Nevertheless, the main body of experimental results reported on this subject indicates that humic substances represent vast majority of the organic matter in most bauxites. Therefore, for the purposes of our work, we will focus our discussion on the oxidation of organic matter arising from humic substances. More specifically, we will suppose that the organic matter to be removed from bauxite has the general structural features of humic substances, discussed below.

Despite intensive research on these substances over many decades,[4] it has not been possible to define the precise structure of humic substances. In general, they consist of complex mixtures of many species[1] including:

1) Humic acids (HAs) containing a complex aromatic core and possessing carboxyl, phenolic, hydroxyl, and alkoxyl functional groups; this component can be extracted into diluted alkali, but precipitates from dilute acid.
2) Fulvic acids (FAs), which are soluble in both alkali and acid.
3) Humins, which are similar in structure to humic acids, but are insoluble in alkali because they form complexes with soil inorganics.

Humic substances can thus be described as assemblies of covalently linked aromatic and aliphatic residues carrying carboxyl, phenolic and alkoxy groups. Figure 1 shows some of the many building blocks found in humic substances, while Figure 2 shows one proposed structure based on pyrolysis studies.[5]

Based on the above information, we have selected the organic substrates listed in Table 1 as suitable model compounds for evaluating the effectiveness of the catalytic systems developed during the course of this project for reducing the organic content of bauxite. There is some indication that species possessing multiple hydroxyl groups can bind minerals in bauxite, thereby resisting removal strategies. The oxidation of alcohol moieties to carboxylic acids will, thus, be of particular interest for our project because decarboxylation of acids should remove the hydroxyl functional groups.

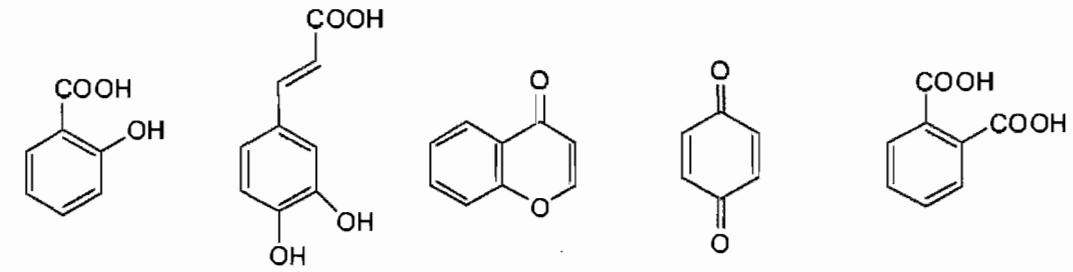


Figure 1: Structures of some building blocks of humic substances (HSs)

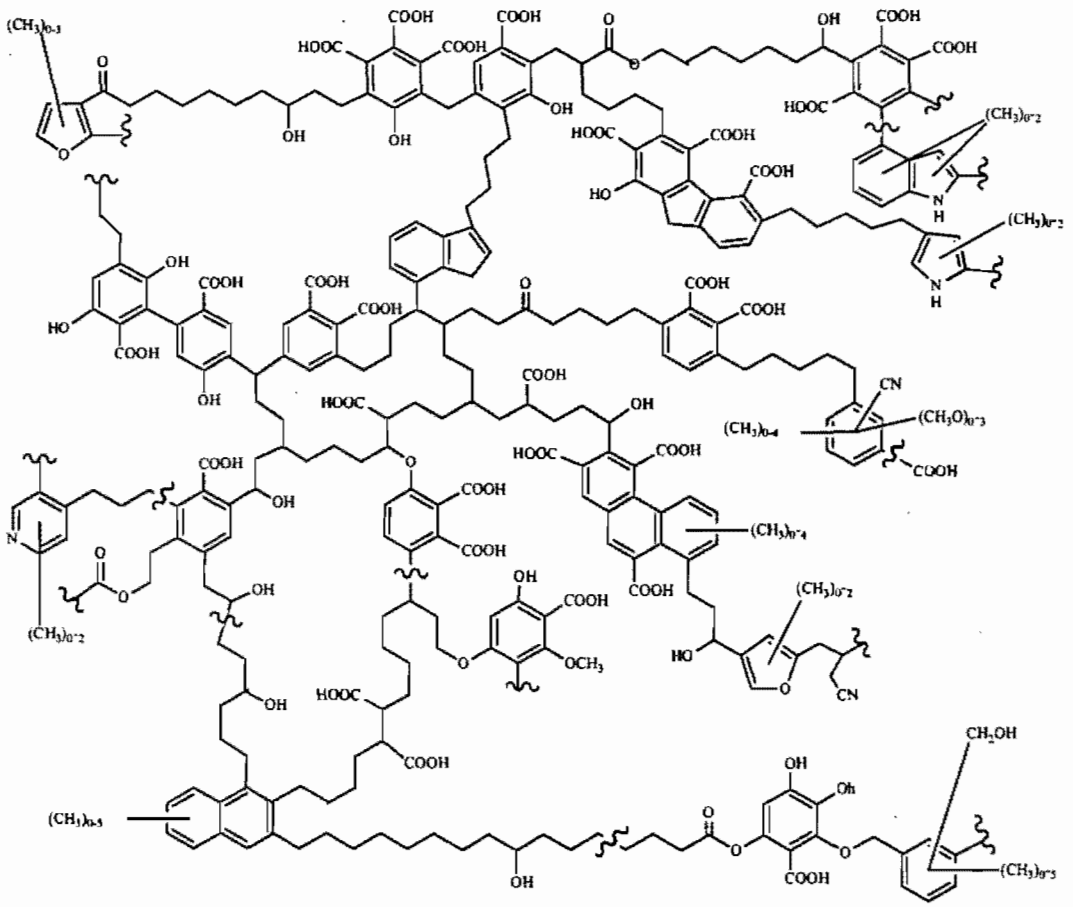
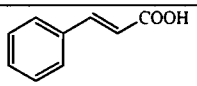
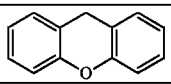
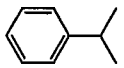
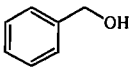
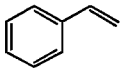
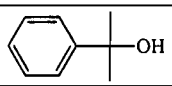
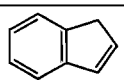
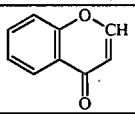
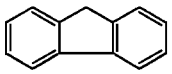
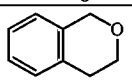
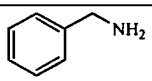
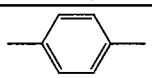
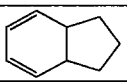


Figure 2: The proposed structure of a humic acid, adapted from Schulten and Schnitzer[5]

Table 1: The model substrates representing the chemical diversity of HSs

Substrate	Structure	Substrate	Structure
trans-Cinnamic acid		Toluene	
Xanthene		Cumene	
Benzyl alcohol		Styrene	
2-Phenyl-2-propanol		Indene	
Chromone		Fluorene	
Isochroman		Benzyl amine	
p-Xylene		Indane	

1.3 Catalytic aerobic oxidations: a literature review

Catalysis is critical to the chemical industry. Sixty percent of today's chemicals and 90 percent of current chemical processes are based on catalytic chemical synthesis. Catalytic oxidation processes make important contributions to many industrial sectors. Catalytic oxidations started to be used during the 1950's and 1960's for the controlled partial oxidation of hydrocarbons; these processes serve to convert oil-, and natural gas-based feedstocks (e.g., alkanes, alkenes, aromatics) to industrial organic chemicals (Figure 3). Some examples of well-known processes are the Wacker process for the oxidation of ethylene to acetaldehyde, the Celanese process for the oxidation of *n*-butane to acetic acid, and the Amoco/Mid-Century process for the production of terephthalic acid from *p*-xylene.

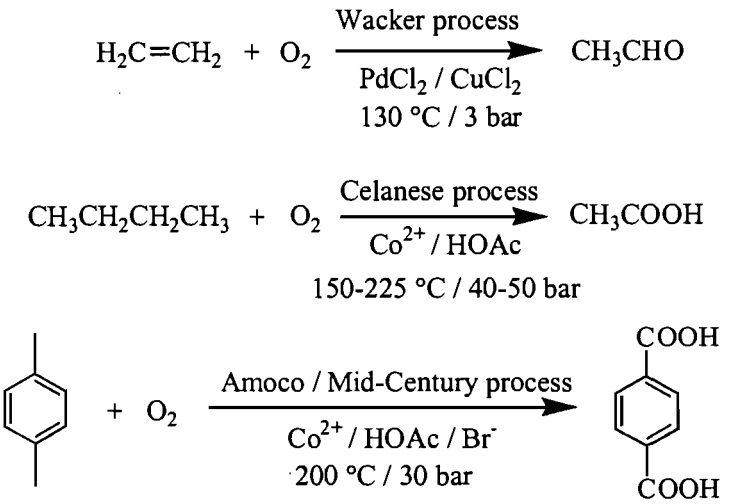


Figure 3: Catalytic oxidations of hydrocarbons

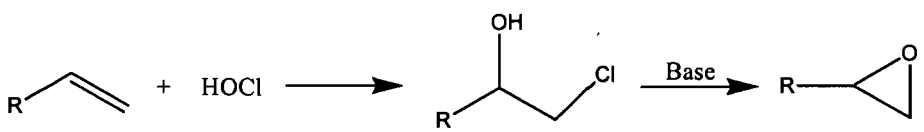
Compared to traditional (non-catalytic) oxidations, catalytic oxidations have three major advantages:

1) Mild conditions. Catalytic oxidations can occur at temperatures and pressures low enough for producers to use economically priced equipment so as to decrease the requirement for the energy and the equipment.
2) Less waste and zero emission. Traditional (non-catalytic) oxidations require stoichiometric quantities of inorganic oxidants such as permanganate or dichromate and generate large amounts of inorganic salt waste than can be toxic and environmentally polluting; in contrast, catalytic oxidations generate much less waste.
3) High selectivity. Catalytic oxidations can ensure that the rate of production of a desired product is greater than the rates of production of undesirable by-products so as to simplify the whole process.

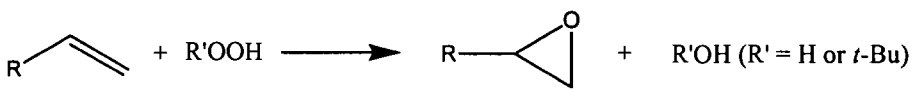
Therefore, from the economic and environmental viewpoints, catalytic oxidations have a huge potential in a number of areas. In the book entitled "Fine chemi-

cals through heterogeneous catalysis", Sheldon has identified four major types of applications: olefin epoxidation; oxidation of alcohols, aldehydes, and carbohydrates; allylic and benzylic oxidation; ammoxidation of aromatic side-chains.[6] These processes are described in the following sections.

Olefin epoxidation. This process is important both in the manufacture of bulk chemicals and also for various transformations in the fine-chemicals industry. For instance, catalytic epoxidation is used for the industrial production of propylene oxide, which is commonly generated by the chlorohydrin method (Eq. 7) and by Halcon method (Eq. 8). In the latter, autoxidation of co-reductants ethylbenzene or isobutene forms reactive hydroperoxides, followed by oxygen transfer from these hydroperoxides to propylene to give the desired epoxide as well as styrene or *t*-butanol co-products. Certain high-valent metal compounds, e.g. Mo^{VI}, W^{VI}, V^{V}, and Ti^{IV}, are used to catalyze this production. These oxidations can also be used for the epoxidation of other olefins that are free of reactive allylic C-H bonds, e.g. butadiene, styrene, nobornene, and *tert*-butyl ethylene.



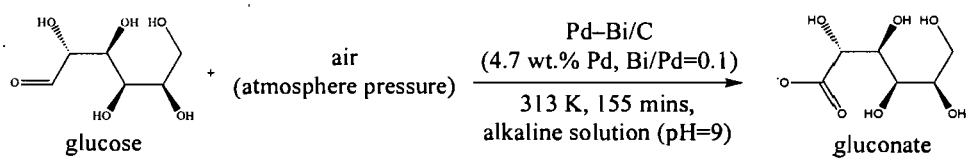
(Eq. 7)



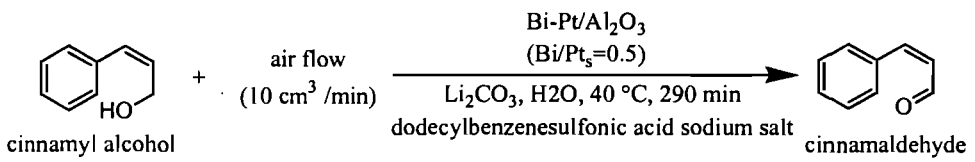
(Eq. 8)

Oxidation of alcohols, aldehydes, and carbohydrates. Oxidation of aldehydes, alcohols or carbohydrate derivatives can be performed with air in aqueous media, in the presence of palladium and platinum catalysts under mild conditions (293–353K and atmospheric pressure). For example, glucose can be oxidized to

gluconic acid with 99.8% selectivity at 99.6% conversion (Eq. 9), whereas cinnamyl alcohol can be oxidized to cinnamaldehyde with 98.5% selectivity at 95.5% conversion (Eq. 10). These are remarkable examples of green chemistry and are attractive for the preparation of specialty or intermediate chemicals employed in the food, cosmetic, pharmaceutical, and chemical industries. The liquid phase oxidation reactions of alcohols on metal surfaces proceed via a dehydrogenation mechanism followed by the oxidation of the adsorbed hydrogen atom with dissociatively adsorbed oxygen.



(Eq. 9)

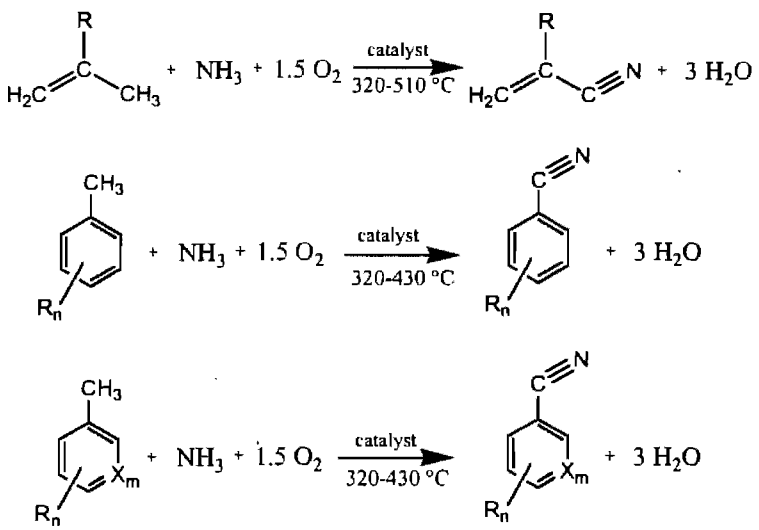


(Eq. 10)

Allylic and benzylic oxidations. Two well-established examples of bulk chemical processes using vapor-phase aerobic oxidations of lower olefins are the oxidation of propylene to acrolein or acrylic acid, and the oxidation of isobutene to methacrolein or methacrylic acid. Palladium-based catalysts appear to be the only heterogeneous catalysts for allylic oxidations. For example, propylene is oxidized to acrylic acid over a Pd/C catalyst at 65 °C in water with 88% selectivity. If this oxidation is carried out in acetic acid with the addition of NaOAc, the oxidative acetoxylation occurs and allyl acetate is obtained with >99% selectivity. Allyl acetate is the raw material for the production of epichlorohydrin and glycerol. Benzylic oxidation of aromatic compounds is also a well-established technology in the

bulk chemicals arena. For instance, toluene is oxidized to benzoic acid, and *p*-xylene is oxidized to terephthalic acid (see the Amoco/Mid-Century process in Figure 3).

Ammoxidation of aromatic side-chains. Ammoxidation refers to the formation of nitriles by oxidation of hydrocarbons with oxygen in the presence of ammonia (Figure 4). Ammoxidation is generally conducted with olefins, or with aromatic or heteroaromatic compounds containing a readily abstractable H atom; this process usually forms allylic or benzylic intermediates. The ammoxidation of lower hydrocarbons is used for the large-scale production of bulk chemicals such as acrylonitrile or methacrylonitrile, whereas the ammoxidation of substituted aromatics or heteroaromatics opens the way for the synthesis of fine chemicals or intermediates for fine-chemical syntheses. A variety of pharmaceuticals, pesticides, dyestuffs, and other speciality products are produced from substituted aromatic or heteroaromatic nitriles.



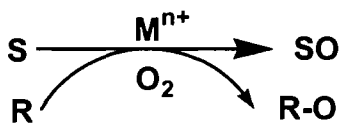
R = H, CH3, halogen, alkoxy, phenoxy, nitro and others,
n = 1-5, X = N, O, S, m = 1-2

Figure 4: Formation of nitriles by ammoxidation of alkenes, methyl aromatic and heteroaromatic compounds

1.3.1 Different categories of oxidations

During these aerobic catalytic oxidations, many reaction mechanisms are involved. Generally they can be classified into the following four categories:

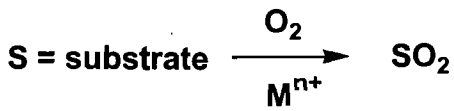
1) **Oxidation based on the model of monooxygenase**. These oxidations are modeled on the natural monooxygenase and require co-reductants such as RCHO, ROH, and PPh_3 that can absorb an oxygen atom from each molecule of O_2 being used in the oxidation of the substrate (Scheme 1).



S = substrate
R = co-reductant

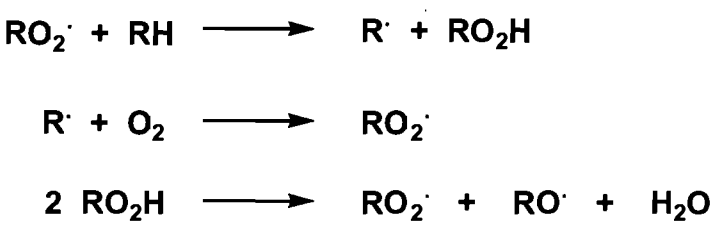
Scheme 1

2) **Oxidation mimicking dioxygenase**. In this reaction both oxygen atoms of the activated molecular oxygen coordinated to the transition metal complex are incorporated into the substrate (Scheme 2).



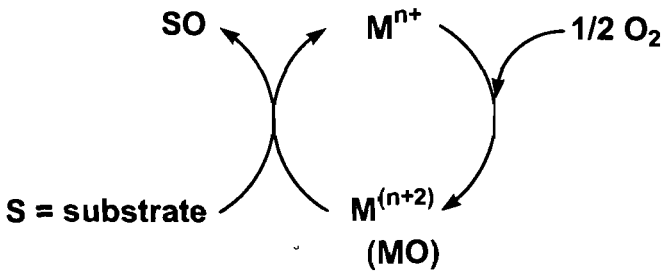
Scheme 2

3) **Free radical oxidation.** These oxidations are generally carried out without any external co-reductants and more closely resemble autoxidation than monooxygenase-catalyzed systems (Scheme 3).



Scheme 3

4) **Oxidation of a coordinated substrate by a metal ion.** In this type of oxidation, the oxidized form of the metal is subsequently regenerated by reaction of the reduced form with molecular oxygen (Scheme 4).



Scheme 4

1.3.2 Literature review of metal-catalyzed oxidation protocols

Because molecular oxygen and air are inexpensive and the main by-product of their reaction is water, these are the ideal primary oxidants. Unfortunately, they are also too weak for oxidizing most substances at near-ambient temperatures and pressures in a timely manner, but this drawback can be minimized by the enhanced oxidative efficiency of metal catalysts. In addition to air or oxygen, a range of relatively cheap, readily available oxidants such as H_2O_2, *t*-BuOOH (TBHP) or NaOCl can be combined with metal catalysts containing a large variety of ligands to give catalytic systems for use in a broad scope of organic syntheses.

A large number of recent reports have shown that oxidation of organic compounds under fairly mild conditions can be catalyzed by transition metal-based reagents operating under aerobic conditions. Of them, reagents based on first-row metals are of particular interest to us both because of their lower expense but also because some of these metals are present in bauxite. In addition, first-row transition

metals tend to promote autoxidation reactions via radical-chain processes. Although the latter are less desirable for applications requiring high selectivities (e.g., traditional organic synthesis), the greater activities of these systems more than compensates for their limited selectivity in the context of degrading organic matter in bauxite.

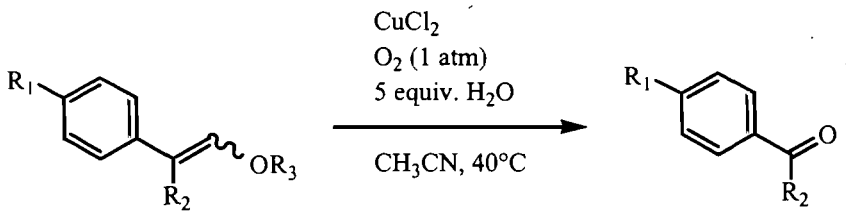
The following section provides specific examples of some of the most promising systems developed recently for the metal-catalyzed aerobic oxidation of organic substrates, which used the complexes of the first-row metals as catalysts. Due to the low cost of dioxygen, this literature review is limited to reports using dioxygen as the main oxidant.

1.3.2.1 Copper catalysts

Cleavage of carbon-carbon double bonds

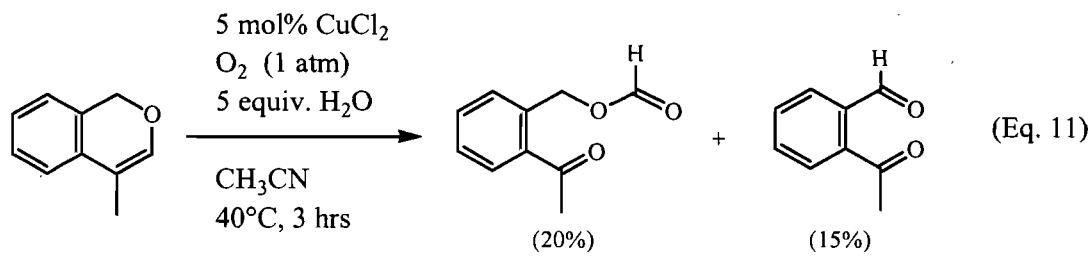
A number of copper compounds are quite effective for the cleavage of C=C moieties in alkenes using molecular oxygen.[7] Tokunaga and co-workers have reported that various aromatic vinyl ethers can be oxidized to ketones by $CuCl_2/O_2/H_2O$ at 40 °C in good yields (Table 2).[8] Furthermore, 4-methyl-1H-isochromene is oxidized to formic acid 2-acetyl-benzyl ester and 2-isopropenyl-benzaldehyde in 20% and 15% yields, respectively (Eq. 11). In this system, it is possible that the reactive reaction involves a radical cation of an enol ether and a dioxetane intermediate; decomposition of the latter would afford a ketone and a formate ester.

Table 2: Oxidative cleavage of C=C bonds in aromatic vinyl ethers[8]



Substrates	R_1	R_2	R_3	$CuCl_2$ (mol%)	Time (h)	Yield of ketone (mol%)*
1a	H	CH_3	CH_3	5	1	86
1b	OCH_3	CH_3	CH_3	1	2	76
1c	CH_3	CH_3	CH_3	1	2	87
1d	Cl	CH_3	CH_3	1	4	68
1e	F	CH_3	CH_3	1	3	63
1f	H	C_2H_5	CH_3	5	2	74
1g	H	$C_{11}H_{23}$	CH_3	5	5	88
1h	H	Ph	CH_3	5	3	92
1i	H	CH_3	$C_{12}H_{25}$	5	3	90

* GC Yield



(Eq. 11)

Oxidation of alkanes and benzylic compounds

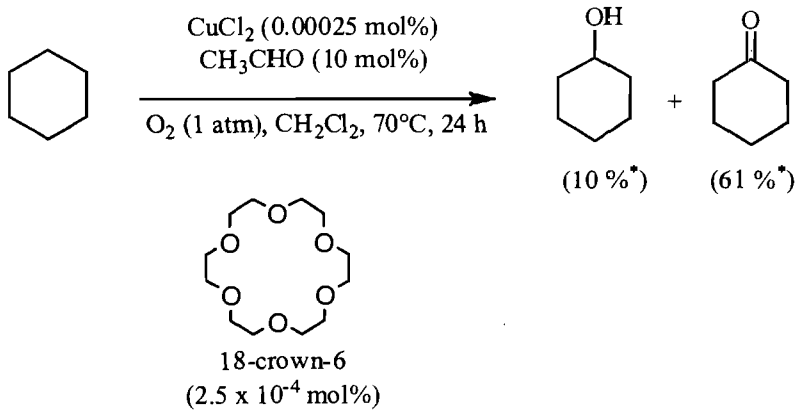
Xu and co-workers reported the oxidation of *p*-cresol to *p*-hydroxy-benzaldehyde or *p*-hydroxybenzoic acid heterogeneously catalyzed by Cu/Mn/C bimetallic oxide catalysts at excellent conversions (>97%). This reaction has been performed in an autoclave in the presence of sodium hydroxide in methanol under ca. 3 atm of dioxygen at 75 °C.[9]

Komiya and co-workers have studied the aerobic oxidation of alkanes and benzylic compounds catalyzed by a combination of copper salts and aldehyde (as co-reductant) under 1 atm of dioxygen.[10, 11] They found, for instance, that an excess of acetaldehyde (3 equiv.) was needed for the aerobic oxidation of cyclohexane catalyzed by ca. 3 mol% of copper salts. The oxidation is thought to involve the following sequence of steps:

1) Aerobic oxidation of the aldehyde generates the corresponding peracid (RCO_3H);
2) The latter then reacts with the copper salt to form highly reactive oxo-copper intermediates of the type Cu^{III}-$O^{\bullet}$ or Cu^{IV}=O;
3) These Cu species abstract $H^{\bullet}$ from the substrate alkane to give Cu-OH species and alkyl radical, which combine to give the corresponding alcohols or ketones.

The need for large excess of the sacrificial aldehyde was attributed to the facile decomposition of the in-situ generated peracids. To minimize this undesirable side-reaction, these authors reasoned that accelerating the reaction of the peracid intermediates with the Cu salts should suppress the decomposition of the peracids. This was attempted by adding to the reaction medium small amounts of crown ethers that should act as electron donating ligands stabilizing the catalytically active high valent copper species. Consistent with this rationale, the presence of small amounts of 18-crown-6 (ca. 2.5×10^{-4} mol%) allowed the use of lower amounts of the copper catalyst (2.5×10^{-4} mol%) and acetaldehyde (10 mol%), as shown in Eq. 12. Thus, a variety of substrates were effectively oxidized to the cor-

responding alcohols and ketones in high turnover number (Table 3; TON = turnover number, mmol of products per mmol of the catalyst used).



(Eq. 12)

Table 3: Aerobic Cu-catalyzed oxidations of alkanes in the presence of 18-crown-6 and acetaldehyde[10]

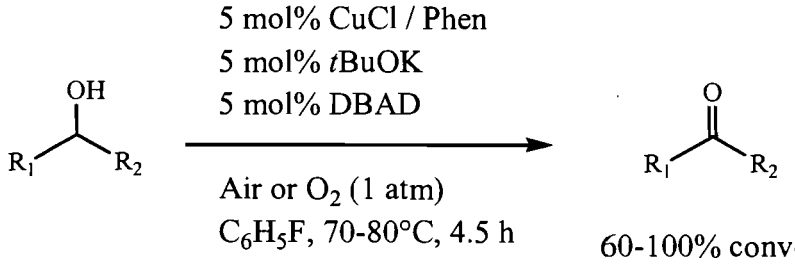
Substrates	Product Yields*		TON
Ethylbenzene	1-Phenylethanol, 2%	Acetophenone, 13%	3480
Indane	1-Indanol, 11%	1-Indanone, 50%	14100
Tetraline	α-Tetralol, 9%	α-Tetralol, 56%	14800
Cyclohexane	Cyclohexanol, 10%	Cyclohexanone, 61%	16200
n-Hexane	2- and 3-Hexanol, 2%	2- and 3-Hexanone, 44%	9770

*Determined by GLC analyses based on the starting acetaldehyde using an internal standard

Oxidation of alcohol

Markó et al. reported that an inexpensive and readily available complex, CuCl·Phen/DBAD (Phen = phenanthroline; DBAD = di-*tert*-butyl azodicarboxylate), is a good catalyst for the aerobic oxidation of a wide range of alcohols into carbonyl derivatives (Eq.3).[12, 13] In this system, the mode of addition of the various partners played a crucial role. For example, adding *t*-BuOK to CuCl/Phen, in the

presence of substrates, followed by the addition of DBAD and heating under a gentle stream of oxygen or air, led to much better conversions.



(Eq. 13)

R_1, R_2 = aryl, alkyl, vinyl, H
DBAD = t-BuO_2C-N=N-CO_2(t-Bu)
Phen = 1, 10-Phenanthroline

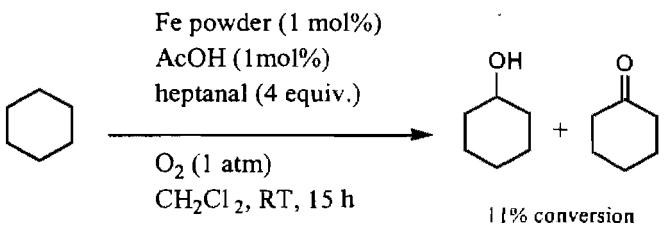
1.3.2.2 Iron catalysts

Iron-catalyzed aerobic oxidations have been investigated for decades and a number of ligands have been found to be most suitable for increasing the oxidation activities of Fe complexes. The use of a co-reductant such as aldehydes, PPh_3, or H_2S is required in most known systems, but some systems work without co-reductants; the latter are believed to operate via a free radical chain mechanism.

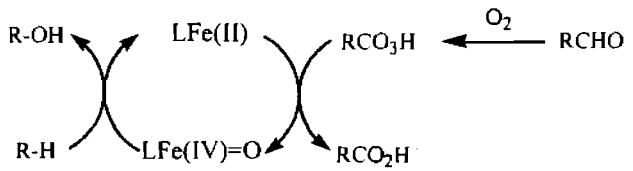
Oxidation of alkanes

A few studies have reported the aerobic oxidation of cyclohexane under atmospheric oxygen (1atm) in the presence of an aldehyde[14, 15]; among the aldehydes studied, heptanal, ^{i}PrOH, and acetaldehyde are the most effective. For example, the combination of iron powder and AcOH in the presence of heptanal as

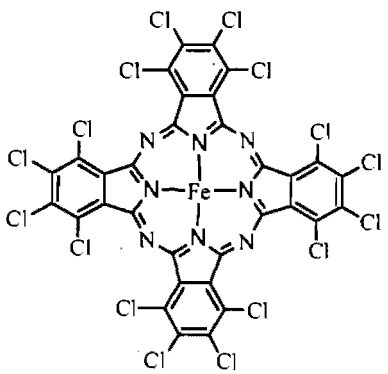
co-reductant catalyzes the room temperature conversion of cyclohexane to cyclohexanol (Eq. 14) with low conversions.[14] Table 4 gives a representative list of Fe-catalyzed reactions studied. The role of the aldehyde in this system is the same as discussed above for the copper complexes (Scheme 5). Other sources of iron examined for this reaction include Fe_2O_3, $FeCl_3$, and complexes **1-3**.



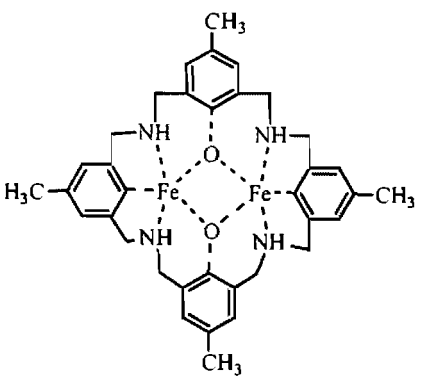
(Eq. 14)



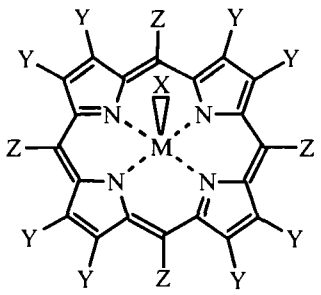
Scheme 5



1



2



3

Metalloporphyrin complexes

3a -- Fe(TPFPP)Cl, M=Fe, X=Cl, Y=H, Z=C_6F_5;
3b -- Fe(TPFPPβ-Br_8)OH, M=Fe, X=OH, Y=β-Br_8, Z=C_6F_5;
3c -- Fe(TPFPPβ-Br_8)N_3, M=Fe, X=N_3, Y=β-Br_8, Z=C_6F_5;
3d -- Fe(TDCPPβ-Cl_8)Cl, M=Fe, X=Cl, Y=β-Cl_8, Z=*o*-$C_6H_4Cl_2$;
3e -- Fe(TTFNMe_2PP)Cl, M=Fe, X=Cl, Y=H, Z=*p*-NMe_2-C_6F_4;
3f -- Fe(TTFOPhPP)Cl, M=Fe, X=Cl, Y=H, Z=*p*-OPh-C_6F_4;
3g -- $[Fe(TPPFPP)]_2O$, M=Fe, X=1/2O, Y=H, Z=C_6F_5;
3h -- Fe(TDCPP)OH, M=Fe, X=OH, Y=H, Z=*o*-$C_6H_4Cl_2$;
3i -- Fe(TDCPPβ-Cl_8)OH, M=Fe, X=OH, Y=β-Cl_8, Z=*o*-$C_6H_4Cl_2$;
3j -- Fe(TDCPPβ-Br_8)OH, M=Fe, X=OH, Y=β-Br_8, Z=*o*-$C_6H_4Cl_2$;
3k -- Mn(TPFPP)Cl, M=Mn, X=Cl, Y=H, Z=C_6F_5;
3L-- Co(TPFPP), M=Co, X=none, Y=H, Z=C_6F_5.

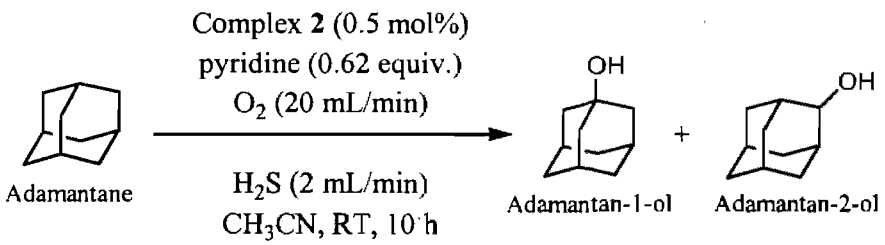
Table 4: Aerobic iron-catalyzed oxidation reactions

Entry	Catalyst	Co-reductant	Other chemicals	Substrates	Ref.
1	Fe powder	heptanal	AcOH	Cyclohexane, *n*-Decane, Adamantane, Ethylbenzene	14
2	Fe_2O_3/TiO_2	^{i}PrCHO	AcOH	Cyclohexane	15
3	**1***	CH_3CHO	--	Cyclohexane	16
4	$FeCl_3$	H_2S	picolinic acid, 4-*tert*-butylpyridine	Cyclohexane, Cyclo-dodecane	17
5	**2***	H_2S	Pyridine	Cyclohexane, Adamantane	18
6	**3b-c***	None	None	Iso-Butane, *n*-propane	19
7	**3a*, 3d-g***	None	None	Ethylbenene, Cumene, (2-Methyl-propyl)-benzene	20
8	**3h-j***	None	$h\nu$ (350-400nm)	Cyclohexane	21
9	γ-$SiW_{10}\{Fe(OH)_2\}_2O_{38}^{6-}$	None	None	Cyclohexane	22
10	$[PW_9O_{37}\{Fe_2Ni(OAc)_3\}]^{10-}$	None	None	Cyclohexane, Adamantane Ethylbenzene	23

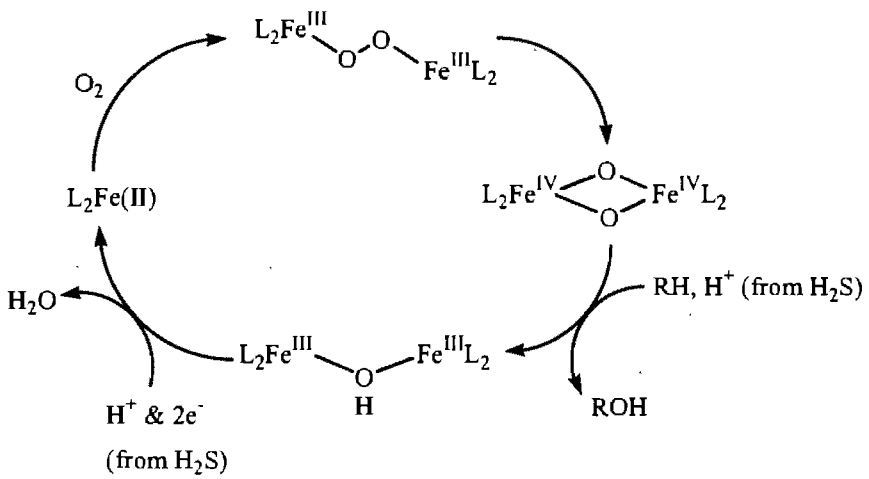
* The structures of Complexes 1-3 are given above.

In 1998, Wang and co-workers reported a new dinuclear iron(II) complex **2** featuring a 24-membered macrocycle containing phenol, pyridine and amino donor groups.[18] This family of complexes served as functional models of the biological oxidant methane monooxygenase (MMO) in that it oxidized many alkanes under

fairly mild conditions. For instance, in the presence of the two-electron reductant H_2S, complex **2** converted adamantane into adamantan-1-ol and adamantan-2-ol with a TON of 27 under mild conditions (Eq. 15). Cyclohexane was also oxidized into cyclohexanol and cyclohexanone with a TON of 31 under similar conditions. The reaction mechanism is proposed to resemble that of MMO oxidations, as follows: these dinuclear Fe(II) complexes react with oxygen to form diiron-peroxide intermediates that decay to a dinuclear Fe(III) complex with an μ–oxo bridge, thus releasing an oxygen atom for hydroxylation of alkanes. Reduction of the dinuclear Fe(III) species with H_2S gives back the initial Fe(II) complex (Scheme 6). In this case, H_2S serves as both an electron and a proton donor, and it is reduced to a sulfur precipitate.



(Eq. 15)

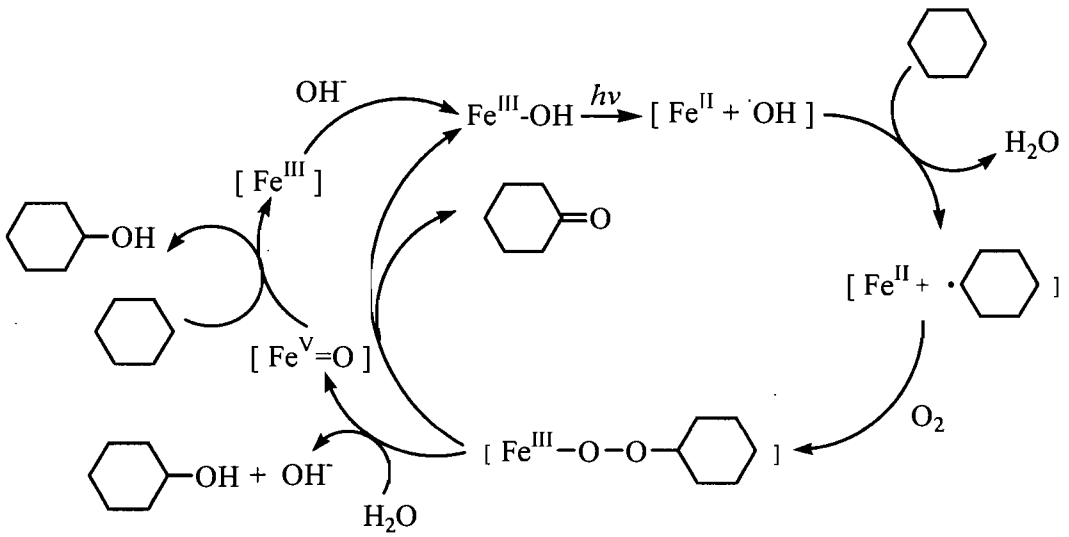


Scheme 6

Metalloporphyrin complexes have long been investigated for their catalytic effects on aerobic oxidation of hydrocarbons in a biomimetic manner. A series of iron-porphyrin complexes have also proved to be versatile systems for catalytic oxidations. In general, iron(III) porphyrins can catalyze two distinctly different aerobic oxidations of organic compounds, one requiring an external reductant to provide two reducing equivalents (Eq. 16, vide infra), and another proceeding via a free radical pathway as in autoxidation reactions. The role of the iron-porphyrin complex in the latter reactions may be to maintain the oxy-radicals necessary for the chain reaction and to decompose the in-situ generated alkyl hydroperoxides.

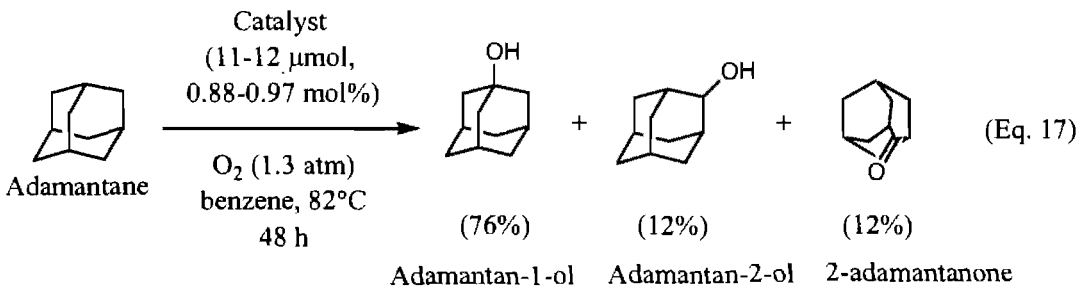
$$RH + O_2 + 2e^- + 2H^+ \rightarrow ROH + H_2O \qquad \text{(Eq. 16)}$$

Free-radical oxidations have been studied by many groups.[19,20] Lyons and co-workers, for instance, have examined the activities of a diverse series of iron-porphyrin complexes **3** (see Scheme 5 above) and shown that complex **3b** can oxidize isobutene at 100 °C to *tert*-butyl alcohol with a TON of 20000, whereas complex **3c** oxidized propane at 125 °C to a mixture of isopropyl alcohol and acetone with a TON of 541.[19] It should be emphasized, however, that the high temperatures required in these reactions lead to the decomposition of these complexes. On the other hand, Maldotti and co-workers have reported that high temperatures can be avoided in the oxidation of cyclohexane by using the *meso*-tetraarylporphyrin-Fe^{III}-OH complexes **3h-j** under irradiation (λ=365nm; ambient temperature; 0.2-1 atm of O_2).[21] The possible mechanism of this reaction is shown in the Scheme 7.



Scheme 7

A novel heterogeneous di-iron(III)-substituted silicotungstate complex, γ–$[SiW_{10}\{Fe(OH)_2\}_2O_{38}]^{6-}$, has been reported for the oxidation of cyclohexane under 1 atm of dioxygen at 83 °C.[22] This reaction was proven to proceed via a radical-chain mechanism such that the addition of N-hydroxyphthalimide (NHPI) (a radical initiator) increased the conversion from 1% to 75% (0.008 mol% cat.; amount of NHPI not given by authors; 1,2-$ClCH_2$-CH_2Cl : CH_3CN = 15:1; 96 h). Another heterogeneous catalytic system has been reported by Mizuno and co-workers[23]: the Keggin-type heteropolyanion complex ($[PW_9O_{37}\{Fe_2Ni(OAc)_3\}]^{10-}$) (tri-transition-metal-substituted) catalyzes the aerobic oxidation of adamantane; 29% conversion and a TON of 25 was achieved at 82 °C and under 1.3 atm of di-oxygen (Eq. 17).



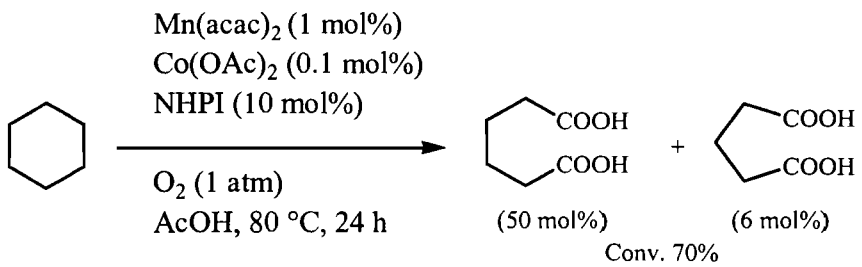
(Eq. 17)

Oxidation of benzylic compounds

Murahashi and co-workers have reported the oxidation of ethylbenzene into a mixture of phenylethanol and acetophenone (20% conversion) catalyzed by Fe powder and aldehydes.[14] The novel iron(II) complex **1** featuring a chlorinated phthalocyanine (see above) can catalyze the oxidation of indane to 1-indanol and 1-indanone; the reaction gives a 95% yield (combined) based on acetaldehyde.[16] As before, the key intermediate in these systems is proposed to be an iron (IV)-oxo species that arises from the reaction of iron complexes with peracids derived from aldehydes and dioxygen. Evans and Smith have studied the oxidation of ethylbenzene (a prototypical free radical autoxidation process) and other aromatic alkanes using Fe(TPFPP)Cl and its derivates (complexes **3a** and **3d-g**, shown above) in a solvent-free system under molecular oxygen at 30-110°C. A mixture of hydroperoxide, phenylethanol, and acetophenone was obtained with TON of up to 25000 using the complex **3g**. The heteropolyanion complex $[PW_9O_{37}\{Fe_2Ni(OAc)_3\}]^{10-}$ can catalyze the oxidation of ethylbenzene under 1.3 atm oxygen at 82°C in a solvent-free system with 17% conversion.

1.3.2.3 Manganese catalysts

Manganese is often used in combination with cobalt to catalyze oxidation reactions. Thus, Iwahama and co-workers have reported[24] that cyclohexane can be oxidized into hexanedioic and pentanedioic acids in good conversions (70%) using a mixture of $Mn(acac)_2$, $Co(OAc)_2$, and NHPI (Eq. 18).



(Eq. 18)

Encapsulation of the trinuclear, μ_3-oxo mixed metal acetato complex $[CoMn_2(\mu_3\text{-}O)(MeCO_2)_6(py)_3]$ (py = pyridine) in zeolite HY has provided a recyclable oxidation catalyst.[25] Thus, the combination of this catalyst with NaBr in H_2O/AcOH can oxidize *p*-xylene to terephthalic acid with 100% conversion and >97% selectivity; the reaction requires high temperatures (ca. 200°C) and high pressures of air (ca. 550 psig). In addition, Murahashi and co-workers have reported that a manganese porphyrin complex **3k** (see above) catalyzes the oxidation of ethylbenzene and other alkanes to the corresponding alcohols and ketones in the presence of acetaldehyde and O_2 (Table 5). The mechanism of this reaction is thought to be similar to the one shown in Scheme 5. A key intermediate, a Mn-oxo species, was generated with O_2 in the presence of acetaldehyde, and shown to promote the oxidation of alkanes to alcohols and ketones.

Table 5: Aerobic oxidations of alkanes catalyzed by the Mn-porphyrin complex Mn(TPRPP)Cl in the presence of acetaldehyde

Entry	Substrates	Yield of alcohol	Yield of Ketone	TON
1	Cyclohexane	Cyclohexanol, 13%	Cyclohexanone, 65%	180
2	*n*-Hexane	2- and 3-Hexanol, 3%	2- and 3-Hexanone, 16%	44
3	Adamantine	1- and 2-Adamantanol, and Adamantan-1,3-diol, 60%	2-Adamantanone, 19%	240
4	Ethylbenzene	1-Phenylethanol, 12%	Acetophenone, 56%	160

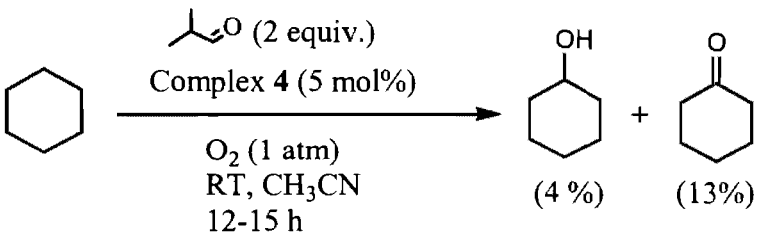
1.3.2.4 Cobalt catalysts

Cobalt salts are effective catalysts for oxidation of a variety of organic substrates, especially in combination with NHPI. As will be seen later, NHPI promoted systems are of particular interest to our project and will be discussed in detail in the section 1.3.2.5, whereas cobalt systems not involving NHPI are discussed in the next three sections.

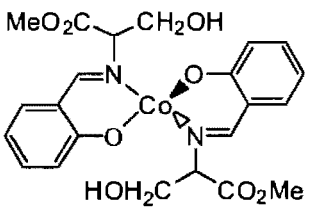
Oxidation of alkanes

Drago and co-workers have reported that the weakly solvated complex $[Co(CH_3CN)_4](PF_6)_2$ catalyzes the oxidation of adamantane and cyclohexane at 75 °C under 3 atm of air; these reactions are believed to proceed via a free radical chain mechanism.[26] Cobalt(II) Schiff base complexes have also been used to catalyze the oxidation of alkanes. For example, the combination of cobalt complex **4** and 2-methylpropanal converts cyclohexane to a mixture of cyclohexanol and cyclohexanone with 17% conversion at ambient temperature and under 1 atm of dioxygen (Eq. 19);[27] an oxo-cobalt species, formed in the presence of aldehydes, is

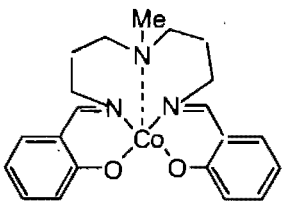
believed to be an intermediate in this reaction. The oxidation of cyclohexane can also be catalyzed by the cobalt-porphyrin complex **3L**.[28]



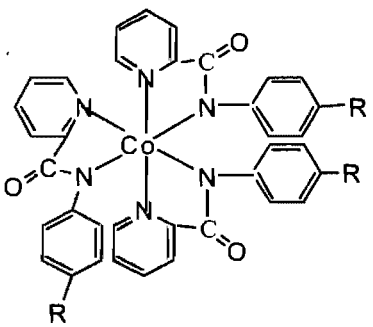
(Eq. 19)



4



CoSMDPT
5



R = H, OMe, Me, Cl

6

Oxidation of alkenes

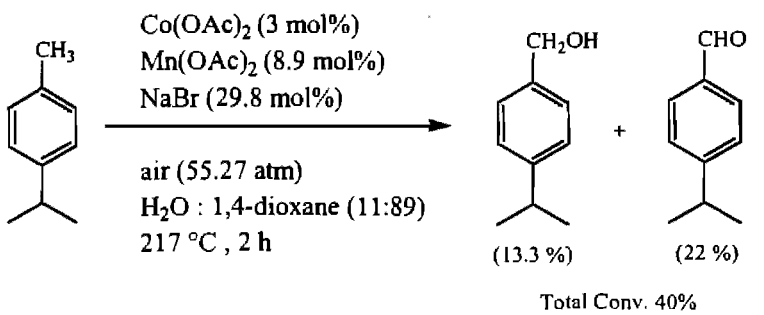
Drago and co-workers have reported that the cobalt complex {Co(SMDPT), **5**, SMDPT = [3-(salicylidineimino)propyl]methylaminato} can catalyze the oxidation of styrene and 1-hexene in the presence of 2-6 atm of molecular oxygen in ethanol at 20-80 °C.[29] The following sequence of events has been proposed to occur in this system:

1) Binding of O_2 to Co(SMDPT);
2) Cobalt-catalyzed oxidation of the primary alcohol solvent to the corresponding aldehyde and hydrogen peroxide (H_2O_2);

3) Formation of a cobalt-hydroperoxy species ($Co^{III}OOH$) by reaction of hydrogen peroxide generated in-situ by Co^{III}(SMDPT);
4) Addition of this Co hydroperoxide species to the olefin to yield an alkylhydroperoxide;
5) Decomposition of the alkylhydroperoxide to ketone and alcohol by Co(SMDPT).

Oxidation of benzylic compounds

The room temperature aerobic oxidation of ethylbenzene, cyclohexane, and adamantane in EtOAc in the presence of acetaldehyde (10 mol%) and O_2 (1 atm) is catalyzed by the cobalt porphyrin complexes **3L** (see Scheme 5).[28] Recently, Qi and co-workers[30] reported that the oxidation of ethylbenzene is catalyzed by the cobalt(III) complexes **6** containing 2-pyridinecarboxamide ligands. Ethylbenzene was mainly converted to acetophenone under 15.79 atm of dioxgyen at 150 °C in good conversion (60–70%). Differently substituted cobalt(III) complexes were compared, and it was found that the parent species (R=H) has the highest catalytic activity. Nair and co-workers[31] have used a catalytic system composed of $Co(OAc)_2$, $Mn(OAc)_2$, and NaBr to oxidize *p*-cymene under high pressure of air and at high temperature (Eq. 20).



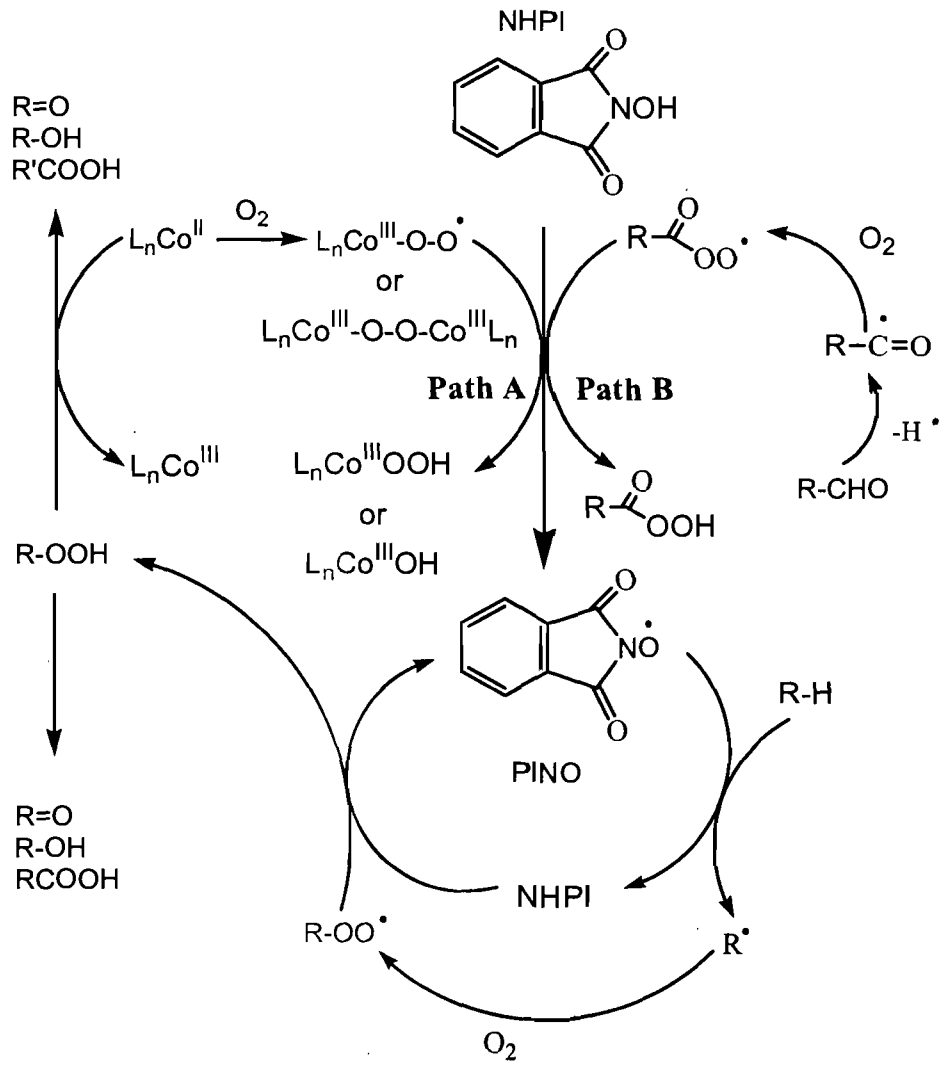
(Eq. 20)

1.3.2.5 Catalytic oxidation by NHPI

NHPI has been recognized as a highly efficient catalyst/promoter for aerobic oxidations under mild conditions of a large variety of organic compounds. NHPI was first used in 1977 by Grochowski and coworkers to catalyze the reaction of ethers with azodicarboxylate and the oxidation of isopropanol with *m*-chloro-perbenzoic acid.[32] In 1986, Foricher and coworkers first reported the use of NHPI in an autoxidation reaction,[33] and then Ishii and co-workers developed the system of NHPI combined with a variable-valence metal, notably cobalt, as an effective catalytic system for the oxidation of a broad range of organic substrates.[34] This system has become known as the 'Ishii system'.

Principle of catalytic aerobic oxidation by NHPI

The main reason why NHPI can promote efficient oxidations is the ease with which it can form the stable phthalimide N-oxyl (PINO) radical. The PINO radical smoothly abstracts a hydrogen atom from hydrocarbons to generate alkyl radicals. The latter are then trapped by O_2 to give alkyl hydroperoxides, which are finally decomposed by Co(III) ions into oxygenated products such as alcohols, ketones, and carboxylic acids. Scheme 8 shows plausible paths for the aerobic oxidation by NHPI-catalytic system.[35]



Scheme 8

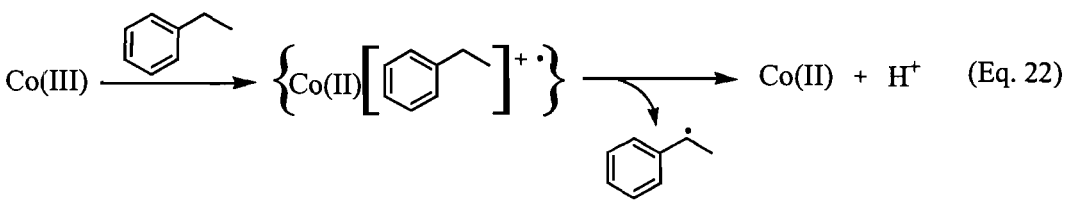
Transition metal ions and aldehydes are generally used to enhance the generation of PINO radicals, which serves to strengthen the efficiency of NHPI-catalyzed oxidation reactions. The high autoxidation rates of aldehydes facilitate their conversion to peroxy radicals; these radicals may in turn oxidize NHPI to phthalimide N-oxy (see path B of Scheme 8). In the NHPI/Co(II)/O_2 system, the complexation of Co(II) with dioxygen generates a labile dioxygen complex such as superoxoco-

balt(III) or μ-peroxocobalt(III) (Eq. 21). These cobalt-oxygen species then facilitate the generation of PINO radicals from NHPI (Path A of Scheme 8).

$$L_nCo^{II} \xrightleftharpoons{O_2} L_nCo^{III}\text{-}O\text{-}O^{\bullet} \xrightleftharpoons{L_nCo^{II}} L_nCo^{III}\text{-}O\text{-}O\text{-}Co^{III}L_n \qquad \text{(Eq. 21)}$$

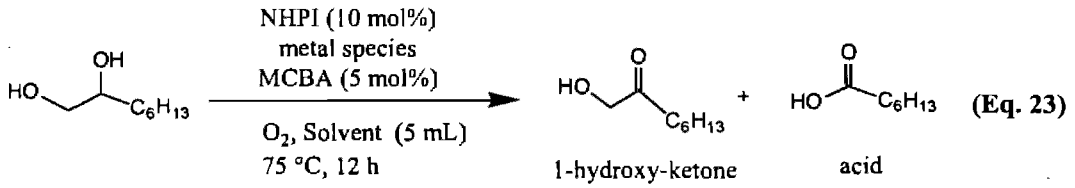
Combination of transition metal salts and NHPI for catalytic aerobic oxidations

$Co(OAc)_2$, $Co(acac)_2$, and $Co(acac)_3$ are often used with NHPI for catalytic oxidations under mild conditions; $Co(OAc)_2$ is, in general, the most effective among these salts. The Co ions have the following two functions in the oxidation reactions: 1) they are converted to oxygenated Co III) complexes that generate PINO radicals; 2) they help the decomposition of hydroperoxide products. Accordingly, $Co(acac)_3$ does not promote oxidation reactions at room temperature, because Co(III) can not form the reactive oxygenated intermediates at low temperatures.[35] On the other hand, Co(III) ions are gradually reduced to Co(II) ions by organic substrates such as toluene and cyclohexane at high temperatures (Eq. 22), and the in-situ generated Co(II) can then react with O_2 to regenerate reactive, oxygenated, high valent intermediates. Hence, the oxidation of ethylbenzene by the NHPI/Co(III) system was initiated after a lapse of 1.5 h at 80°C.[36]



(Eq. 22)

Very interestingly, Iwahama et al. reported that 1,2-octanediol is oxidized to the one-carbon-less oxidized product heptanoic acid in good selectivity (Table 6) by the NHPI/O_2 system when $Co(acac)_3$ was used instead of $Co(OAc)_2$ (Eq. 23).[37]

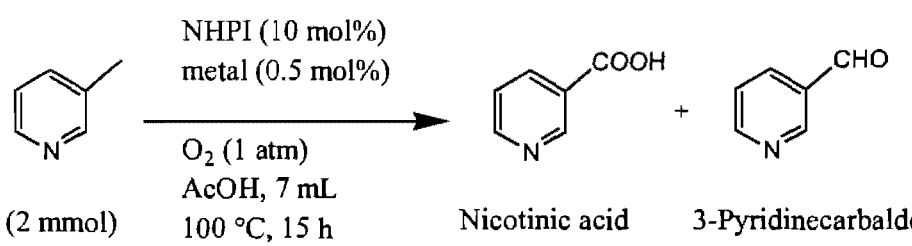


(Eq. 23)

Table 6: Oxidations of 1,2-octanediol with O_2

Solvent	Co species	Conv. (mol%)	Yield of 1-hydroxy-ketone (mol%)	Yield of acid (mol%)
EtOAc	$Co(OAc)_2$, 0.5 mol%	44%	27%	10%
CH_3CN	$Co(acac)_3$, 1 mol%	83%	7%	71%

Shibamoto et al. have studied[38] the oxidation of 3-methylpyridine to compare the reactivities of several systems consisting of combinations of various transition metal salts with NHPI (Eq. 24). As seen from the results listed in Table 7, Cobalt salts afforded the best oxidation rates. Since combinations of Co and Mn ions are effective for the autoxidation of hydrocarbons,[39] Shibamoto et al. have also examined the influence of Mn ions on the oxidation of 3-methylpyridine by the NHPI/$Co(OAc)_2$ system. Table 8 shows that $Mn(OAc)_2$ has only a small effect on the oxidation reaction when fairly high loadings of $Co(OAc)_2$ are used (runs 1 and 2), but a remarkable enhancement in the catalytic activity is observed with low loadings of $Co(OAc)_2$ (runs 6 and 8).



(Eq. 24)

Table 7: The effect of metal salts on aerobic oxidations of 3-methylpyridine catalyzed by NHPI

Run	Metal salts	Conversion (mol%)	Yield of Nicotinic acid (mol %)	Yield of 3-Pyridinecarboxaldehyde (mol%)
1		0	---	---
2	$Co(OAc)_2$	60	53	1
3	$Co(acac)_2$	46	43	1
4	$Mn(OAc)_2$	3	Trace	---
5	$Cu(OAc)_2$	5	2	---
6	$VO(acac)_2$	2	---	---
7	$Fe(acac)_3$	8	1	---
8	$Ni(OAc)_2$	3	---	---

Table 8: The effect of $Mn(OAc)_2$ on aerobic oxidations of 3-methylpyridine by $Co(OAc)_2$/ NHPI[a]

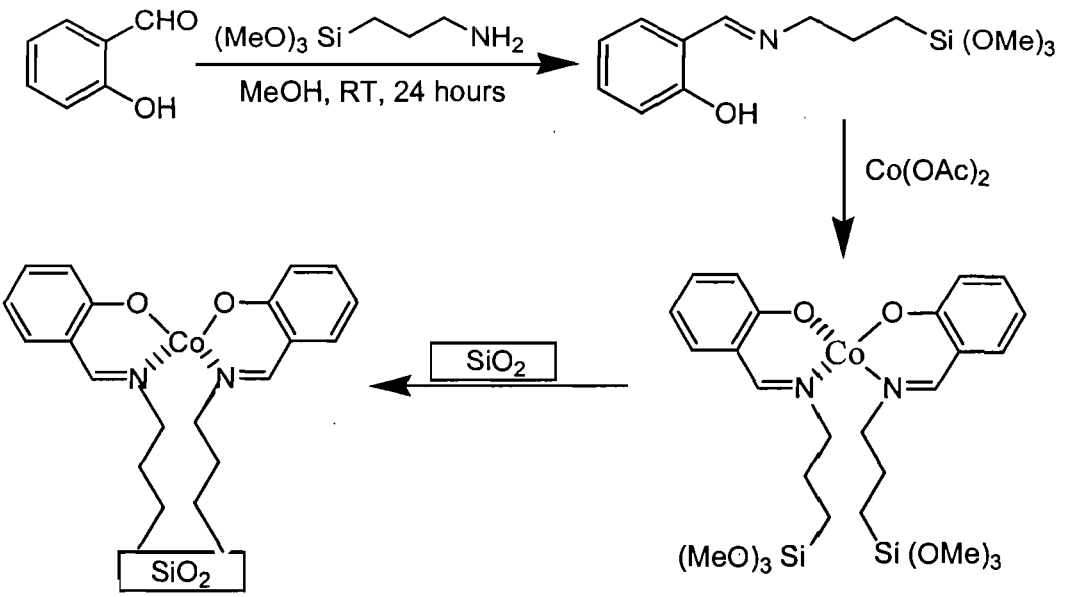
Run	$Co(OAc)_2$ (mol%)	$Mn(OAc)_2$ (mol%)	Conv. (mol%)	Yield of Nicotinic acid (mol %)	Yield of 3-Pyridinecarboxaldehyde (mol%)
1	1.5	---	82	76	2
2	1.5	0.1	80	74	1
3	1.0	---	67	72	1
4	1.0	0.1	77	63	1
5	0.5	---	60	53	1
6	0.5	0.1	78	73	1
7	0.1	---	5	4	---
8	0.1	0.1	48	41	1
9	0.1	0.5	72	65	2
10[b]	0.5	0.1	65	62	2

[a] **Procedure:** 2 mmol of 3-methylpyridine were allowed to react with O_2 (1 atm) in the presence of NHPI (10 mol%), $Co(OAc)_2$, and $Mn(OAc)_2$ in acetic acid (7 mL) at 100 °C for 15 h.

[b] The reaction was carried out using 10 mmol of 3-methylpyridine in 35 mL of AcOH.

Although the $Co(OAc)_2$/NHPI system is fairly efficient, requiring loadings of ca. 0.1 % Co(II) only, for some applications a greater efficiency would be required from a practical point of view. In this sense, recycling of the catalysts would be desirable. Rajabi et al. have developed a recyclable heterogeneous silica based co-balt complex to resolve this problem (Scheme 9).[40] The use of this cobalt catalyst

with NHPI showed high oxidation rates (over 85% yields) for a variety of benzylalcohols and alcohols; moreover, this system has a much higher thermal stability, and it could be recovered and reused for at least five reaction cycles without considerable loss of reactivity.



Scheme 9

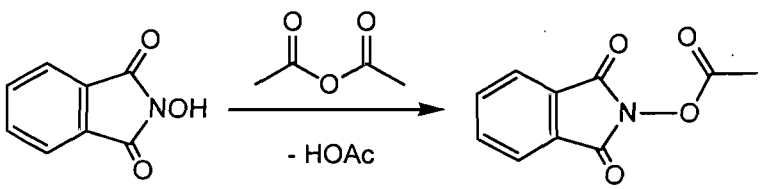
N-Hydroxy phthalimide derivatives and analogues

Given the important role of NHPI in aerobic oxidation systems, a number of groups have investigated the efficacy of NHPI derivatives in order to delineate the influence of various structural features on the chemistry of this species. The following pragraphs discuss the available data on three types of derivatives of NHPI.

1) N-acetoxyphthalimide (NAPI)

Since NHPI undergoes gradual decomposition under aerobic oxidation conditions, its efficacy for the oxidation reaction is likely compromised. The acyl derivative of NHPI, *N*-acetoxyphthalimide, NAPI, which is easily prepared by the

reaction of NHPI with acetic anhydride (Eq. 25), is somewhat more resistant to decomposition.[41] The reaction of NAPI with the residual water present in the reaction medium or formed during the oxidation reaction serves as a 'slow release' mechanism for the in-situ generation of NHPI. A number of studies have indicated that NAPI is more effective than NHPI. For example, the oxidation of *p*-xylene with NHPI/Co/Mn under mild conditions (100 °C, 1 bar O_2) required a larger amount of NHPI (20 mol%), presumably because of the decomposition of NHPI; in contrast, only 5 mol% of NAPI gave comparable results.[42]



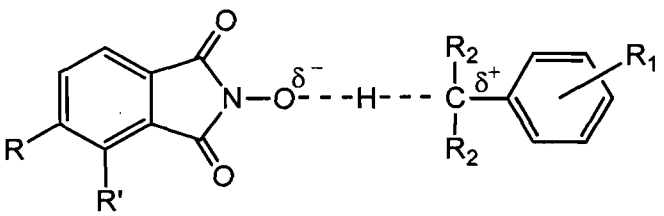
NHPI NAPI (Eq. 25)

2) Substituted NHPI derivatives

The rate of catalytic oxidations promoted by variously substituted derivatives of NHPI has been studied recently. Generally, two types of aryl substituents have been examined; electron donating groups and electron withdrawing groups. Wentzel et al.[43] reported that electron withdrawing substituents on NHPI accelerated the oxidation of ethylbenzene, while electron donating groups decreased rates of oxidation. They propose that the polar transition state model explains the observed substituent effects because an electron-withdrawing substituents on NHPI (R, R') should stabilize a partial negative charge on the hydroxy oxygen atom, as illustrated below (Figure 5). Annunziatini et al. confirmed that introducing electron-withdrawing substituents in the NHPI aryl ring increased the catalytic effi-

ciency of oxidation. This was done by competitive oxidations with a series of aryl-substituted NHPIs, in addition to the kinetic isotope effect studies and the determination of O-H bond dissociation energies (BDEs) with using the EPR technique.[44] However, the same authors state in another article that lignin model compounds and delignification of wood pulp were facile using NHPI bearing electron donating substituents.[45] Evidently, these two statements are contradictory and this issue remains ambiguous requiring further study.

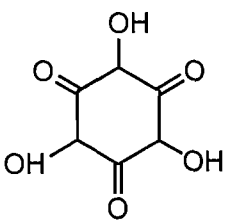
Figure 5: Transiton state for the reaction of PINO with substituted benzenes



R_1 = H, OMe, Me, Br, etc.
R_2 = H, Me, OH

3) NHPI analogues: N, N', N"-Trihydroxyisocyanuric Acid (THICA).

THICA appears to be a more efficient catalyst than NHPI for the aerobic oxidation of alkylbenzenes,[46] as illustrated by the facile oxidation of a variety of *meta*- and *para*-substituted toluenes bearing an electron withdrawing substituents. Thus, the combination of THICA (5 mol%) and $Co(OAc)_2$ (0.5 mol%) allowed the smooth oxidation of these species to the corresponding benzoic acids in almost quantitative yields under ambient pressure of O_2 at 100 °C. One limitation is the requirement for high temperatures: no oxidation was observed with THICA at room temperature. This is believed to be due to the higher O-H



THICA

bond dissociation energy for THICA (91.6 kcal/mol) compared to that of NHPI (88.1 kcal/mol).

Applications of catalytic oxidations by NHPI

1) Oxidation of alcohols

Iwahama et al. have reported a highly efficient catalytic oxidation of alcohols by Co/NHPI/O_2 under mild conditions (Table 9).[37] The oxidation of secondary alcohols by NHPI/$Co(OAc)_2$/MCBA (*m*-chlorobenzoic acid) was particularly facile and afforded the corresponding ketones in good to excellent yields. It was found that benzoic acids such as MCBA enhance the oxidation of alcohols by promoting the decomposition of alkylhydroperoxide by $Co(OAc)_2$, but the precise role of MCBA in the aerobic oxidation by the NHPI/Co(II) system has not been explained by Iwahama et al.

These authors have also reported the oxidation of various diols to α-ketols, diketones or cleaved products (aldehydes or carboxylic acids).[37] As can be seen from the results listed in Table 10, acyclic vic-diols give primarily diketones, cyclic vic-diols give 1,2-diketones or dicarboxylic acids (cycle cleaving), terminal 1,2-diols give carboxylic acids, and 1,3 and 1,4-diols give hydroxyl ketones.

Table 9: Aerobic oxidations of secondary alcohols by $Co(OAc)_2$ / NHPI / O_2

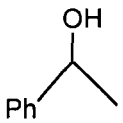
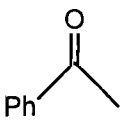
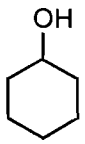
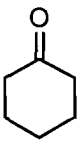
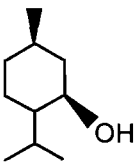
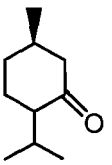
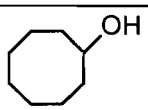
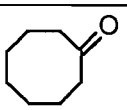
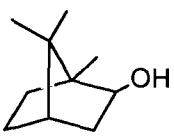
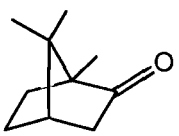
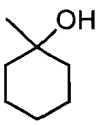
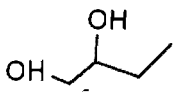
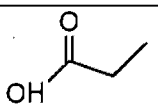
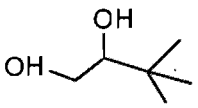
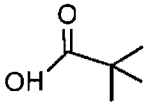
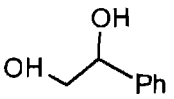
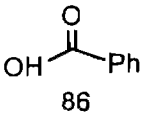
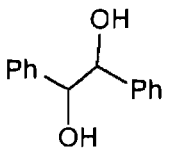
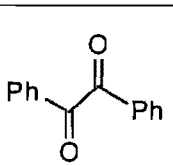
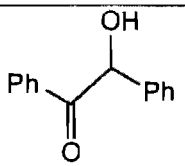
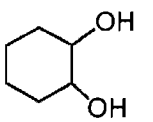
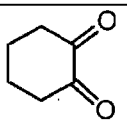
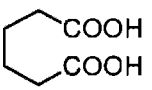
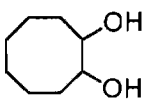
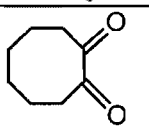
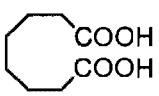
Substrate	Time (hours)	Conversion (mol%)	Product	Yield (mol%)
	15	100		98
	20	86		83
	20	59		47
	15	97		94
	20	91		91
	20	No reaction		

Table 10: Aerobic oxidations of diols by $Co(acac)_3$ / NHPI / O_2

Substrate	Time (hours)	Conv. (mol%)	Product(s), Yield(s) (mol%)
	13	80	 70
	13	89	 71
	20	96	 86
	20	97	 84  12
	20	62	 26  30
	20	94	 42  44

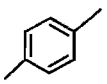
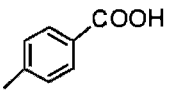
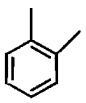
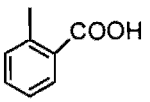
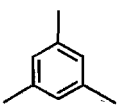
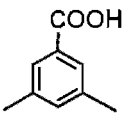
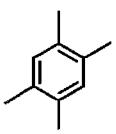
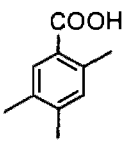
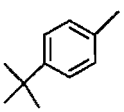
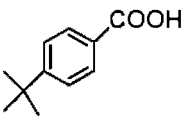
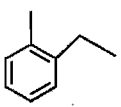
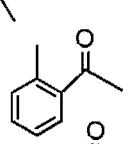
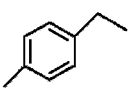
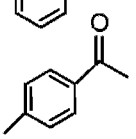
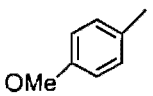
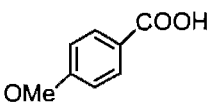
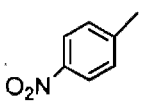
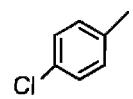
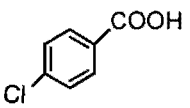
2) Oxidation of aromatic compounds

A. Oxidation of alkylbenzenes

Yoshino et al. have reported an effective method for catalytic oxidation of alkylbenzenes with molecular oxygen under ambient pressure and at room temperature.[35] For instance, toluene is oxidized to benzoic acid in 81% yield by NHPI/$Co(OAc)_2$/O_2 at room temperature. Under these conditions, *o*- and *p*-xylenes were selectively converted into the corresponding monocarboxylic acids (over

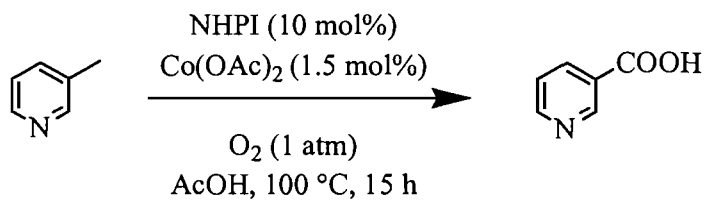
80% yields) without the formation of the dicarboxylic acids (Table 11). The electronic properties of the substituents on the aromatic ring affect the oxidation rate, as seen from the difficult oxidation of *p*-nitrotoluene.

Table 11: Aerobic oxidations of alkylbenzenes by $Co(OAc)_2$ (0.5 mol%) / NHPI (10 mol%) / O_2 (1 atm) at 25°C

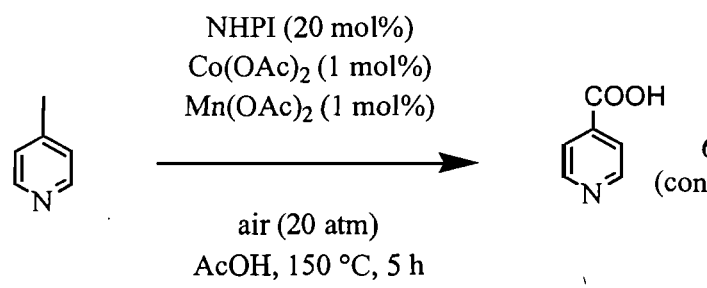
Substrate (3mmol)	Solvent	time (h)	conv. (%)	main product (yield %)	
	AcOH	20 h	95		85
	AcOH	20 h	93		83
	AcOH	20 h	81		51
	AcOH	12 h	100		93
	AcOH	20 h	95		91
	CH_3CN	20 h	82		37
	CH_3CN	20 h	87		47
	CH_3CN	6 h	89		80
	no reaction				
	AcOH	20 h	71		67

B. Oxidation of methyl-pyridines and methyl-quinolines

Mukhopadhyay and Chandalia have reported the first successful catalytic oxidation of β-picoline.[47] The reaction of this substrate in acetic acid with NHPI (10 mol%) and $Co(OAc)_2$ (1.5 mol%) under O_2 (1atm) at 100 °C for 15 h afforded nicotinic acid with 82% conversion and 76% yield (Eq. 26). γ-picoline was more difficult to oxidize, but after optimization of the reaction conditions it was possible to obtain 4-pyridinecarboxylic acid in good yields (Eq. 27).



76% (conv. 82%) (Eq. 26)



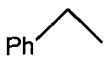
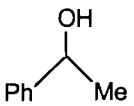
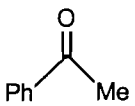
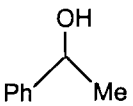
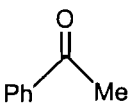
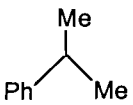
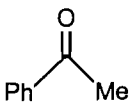
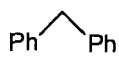
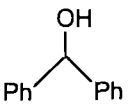
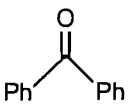
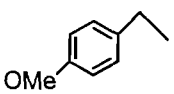
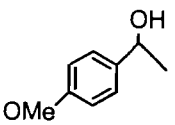
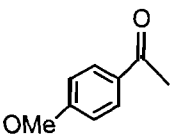
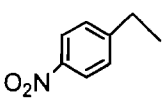
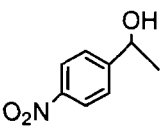
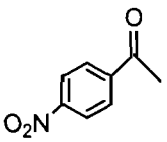
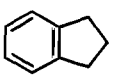
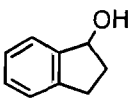
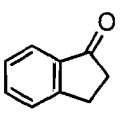
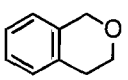
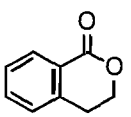
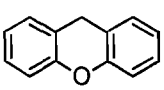
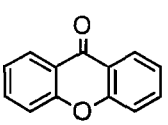
60% (conv. 67%) (Eq. 27)

The above results are in contrast to those reported by Wentzel et al. who maintain that heteroaromatic analogues can not be oxidized by NHPI/Co/O_2. For instance, these authors found that treatment of 3-methyl-quinoline by the NHPI-Co-Mn system under the reaction conditions used for the β-picoline oxidation did not result in any oxidation at all. They speculate that a nitroxide or sulfoxide is formed to deactivate the oxidants, or that coordination of the sulfur or nitrogen atoms of the substrates to the Co species can occur to hamper this oxidation in some manner.[43]

C. Oxidation of benzylic compounds

Benzylic compounds are quite prone to oxidations and many can be oxidized under ambient pressure of dioxygen catalyzed by NHPI in combination with acetaldehyde in the absence of a transition metal species (Table 12).[48]

Table 12: Aerobic oxidations of benzylic compounds (1 mmol) by NHPI (0.1 mml) and acetaldehyde (1 mmol) at room temperature

Substrate	time (h)	conversion (%)	product(s), yield(s) (%)			
	5	48		4		41
	21	97				90
	72	37				37
	10	49		10		36
	10	24		2		22
	10	70		4		66
	19	75		46		29
	10	99				94
	19	94				70

Conclusions on the oxidation reactions promoted by NHPI

The above discussion shows that NHPI is a highly effective catalyst for the aerobic oxidation of a large number of hydrocarbons. The action of NHPI can be facilitated by aldehydes or a number of metal salts, of which Co species on their own or in combination with Mn compounds are the most effective. The presence of cobalt species facilitates the oxidation of a fairly wide variety of organic compounds, whereas the beneficial properties of aldehydes as co-oxidants apply to a limited range of compounds. In addition, both metal catalysts and aldehydes have certain drawbacks, including the following:

- Aldehydes tend to decompose by in-situ autoxidation reactions, which reduces the overall efficiency of the oxidation protocol (one or more equivalents of aldehydes is necessary for oxidizing most substrates) and renders these reactions less reproducible; moreover, aldehydes and their oxidized products become impurities in the system that must be separated.
- Transition metal species can be expensive and difficult to recycle; furthermore, oxidation of some substrates containing some functional groups such as amines is complicated by the binding of the functional group to the metal centre.

1.4 SCOPE OF THE JOINT UdeM-ALCAN PROJECT

Organic materials present in bauxite can cause numerous problems during the various stages of the Bayer process for alumina purification. This project aims to find a way to eliminate or reduce the organic contents of bauxite before subjecting it to the Bayer process. From both the economic and environmental points.of view, an attractive method for achieving this objective is the catalytic aerobic oxidation of organic matter. Our long-term objectives are, therefore, to develop an effective system for the catalytic oxidation of relevant organic substrates and apply this system to the degradation of organic matter in bauxite.

The present thesis can be divided into two main parts. The first part of this chapter summarized the commonly accepted knowledge on the general features of HSs and identified those structural characteristics and functional groups that will be the target of the oxidative degradation strategy employed in our project. It also gives a review of the recent literature on the various catalytic systems for oxidizing organic matter under aerobic conditions. These sections should familiarize the reader with underlying motivations for the UdeM-Alcan project and the rationale for the type of experimental studies undertaken by the researchers at UdeM. The second part of the thesis describes the experimental work, which consists of aerobic oxidations of organic substrates based on the combinations of Co(II)/O_2/NHPI. This section will describe the studies aimed at examining the catalytic efficiency of various metal salts and optimization of various parameters such as temperature, air/O_2, solvent, etc. In the last part of the work, the catalytic systems were used on aerobic oxidations of humic acids or bauxite.

When devising a strategy for developing a system for catalytic oxidative degradation of organic matter in bauxite, it should be noted that the nature of the oxidation reactions to be performed in this system are significantly different from the oxidation of relatively pure samples of organic compounds. In the latter context, chemical selectivity (i.e., conversion of a given functional group to a specific one) and efficacy (i.e., yields and catalytic turnover numbers) are the ultimate criteria. In contrast, when treating bauxite we are dealing with a large number of poorly defined compounds to be oxidized for the purpose of breaking up the complex humic network in order to render it more soluble in mildly alkaline media. While efficacy of the system in terms of oxidation yields is important, many other factors deserve more consideration, including cost of reagents, temperature, pressure of oxygen, solvents, reaction time, etc. Therefore, the system to be developed must be selected with the objective of providing a simple protocol requiring fairly inexpensive reagents and mild reaction conditions.

The choice of metal should be limited to those that are either very inexpensive or, ideally, exist in bauxite. In other words, we should be considering systems based on either iron, cobalt, or copper. The oxidant of choice is air (ideal) or oxygen, preferably at ambient pressures. The co-oxidants or additives should be inexpensive and ideally water-soluble; their actions should be fairly efficient in order to allow relatively short reaction times.

The above considerations have convinced us that the cobalt/NHPI/O_2 system would be a good starting point for our development studies. The lower abundance of cobalt in bauxite compared to iron is compensated by the requirement of very small amounts of cobalt (less than 0.5%) and the mild conditions its reactions

need. In addition, cobalt systems do not require expensive ligands such as the porphyrins needed for the iron systems. Although the need for running Co-catalyzed oxidations in the presence of NHPI runs counter to our goal of ridding bauxite of its organic content, it should be noted that this compound is somewhat soluble in water, especially in alkaline solutions, and should not remain in the samples beyond the initial extraction phase. We also explore the possibility of preparing NHPI derivatives that are more soluble in aqueous media. Finally, literature results have indicated that the Co/NHPI/O_2 system is quite amenable to modifications and it is hoped that optimization reactions will allow a more suitable system to be developed for oxidative degradation of the organic species in bauxite.

Therefore, we propose to design and carry out optimization experiments based on the cobalt/NHPI/O_2 system for the catalytic aerobic oxidation of the above-noted model compounds. The main points for the initial optimizations will be the reaction conditions (temperature, pressure, nature of oxidant, air or oxygen), reaction medium (aqueous or organic solvents), role of pH (possibility of doing oxidations in dilute alkaline solutions), and amount of cobalt and NHPI required for an efficient and general oxidation. We will also explore the possibility of substituting cobalt by iron combined with NHPI at the second phase of our studies. Although the effectiveness of iron salts combined with NHPI is much less than the cobalt, rich iron salts in the bauxite can compensate this drawback. Then at the third phase of our studies, we research the possibilities of iron salts or cobalt acetate combined with NHPI derivatives that are more soluble in water. At the end, the NHPI systems are explored on aerobic oxidations of humic acids or bauxite.

Chapter 2 : EXPERIMENTAL SECTION

2.1 General

Most of the chemicals used in our studies, including cobalt acetate, NHPI, and the target substrates listed in Table 1 were purchased from commercial sources and used as received without further purification. Table 13 lists the grade and suppliers of all chemicals. All catalytic aerobic oxidation experiments were performed under 1 atm of air or oxygen; the latter was obtained in compressed cylinders (99.99%) from commercial sources. Oxidized products of the experiments, except bauxite and humic acid sodium salt, were analyzed both qualitatively and quantitatively by NMR and/or GC-MS, as described below. UV-vis spectroscopy was applied to monitor oxidations of the bauxite and humic acid sodium salt. The UV-vis spectrophotometric analysis was conducted on Cary 500i UV-vis-NIR spectrophotometer. The samples were dissolved in distilled water and placed in a 1-cm quartz window cuvette and scanned from 800 to 200 nm.

NMR Analyses. ^{1}H NMR spectra were obtained on Bruker ARX400 and AMX300 NMR spectrometers (400 and 300 MHz respectively). The samples were prepared by evaporating a quantitative volume (0.2-1 mL) of the stock solution to dryness and dissolving it in $(CD_3)_2SO$, $CDCl_3$, or C_6D_6. Calibration of the spectra was done against the residual solvent signals (7.16 ppm for C_6D_5H, 2.50 ppm for CD_2HSOCD_3, and 7.26 ppm for $CHCl_3$); in addition, a portion of hexamethyl ben-

zene (3-5 mg) was added to the sample as an internal standard for quantifying the results.

Table 13: List of chemicals used

Chemicals	Supplier	Grade	Conc.
Toluene	Aldrich	ACS	99%
Styrene	Aldrich		99%
Cumene	Aldrich		98%
Benzaldehyde	Aldrich		99+%
Benzyl amine	Aldrich		99%
Benzyl alcohol	Fisher		≥ 98%
Indane	Aldrich		95%
2-Phenyl-2-propanol	Aldrich		97%
Benzoic acid	BDH Chemicals	Analytical	99,90%
Isochroman	Aldrich		99%
1-Indanone	Aldrich		99+%
Indene	Aldrich	Technical	90%
Trans-Cinnamic acid	Aldrich		97%
Xanthene	Aldrich		99%
Fluorene	ACROS Organics		98%
Chromone	Aldrich		99%
N-hydroxyphthalimide	Aldrich		97%
Cobalt acetate	Fisher	Certified	
Acetonitrile	Aldrich	ACS	≥ 99,5%
Acetone	Aldrich	ACS	≥ 99%
Dioxane	Aldrich	ACS	≥ 99%
Tetrahydrofuran	Aldrich	ACS	≥ 99%
Tetrabutylammonium bromide	Aldrich		99%
Hexamethyl benzene	Estman Organic Chemicals	Chemical purpose	
4-Cl-Benzoic acid	Aldrich		99%
Chloroform-d	Aldrich		99,8 atom % D
Benzene-d	Aldrich		99,8 atom % D
(Methyl sulforxide)-d_6	Aldrich		99,9 atom % D
Sodium dodecylsulfate	Aldrich	GC	≥ 98,5%
Benzalkonium chloride	Aldrich		
p-Xylene	Aldrich		99%
Humic acid, sodium salt	Aldrich	Tech.	
Humic acid	Fluka	Tech.	
1-Indanol	Aldrich		98%
Ferrous sulfate	A&C America chemicals Ltd.	ACS	99+%

Chemicals	Supplier	Grade	Conc.
Ferric nitrate (strong oxidant)	Fisher Scientific Company	ACS	
Ferrous chloride (crystal)	Anachemia Chemicals		≥ 99,5%
Ferric chloride	Aldrich	A.C.S / reagent	97%
Iron(II) acetate	Aldrich		95%
Ferric oxide	J. T. Baker Chemical Co.	Analyzed' reagent	99,8%
Iron(III) acetylacetonate	Students' product		
Palladium on carbon 10 wt.%	Aldrich		
Magnesium sulfate	A&C America chemicals Ltd.	Reagent	99,5%
Sodium hydrocarbonate			
Sodium hydroxide			
Acetic anhydride	Aldrich		99,5%
4-Nitrophthalic anhydride	Aldrich		92%
4-Nitrophthalimide	Aldrich		98%
O-Benzylhydroxylamine hydrochloride	Aldrich		99%
Diphenyl carbonate	Aldrich		99%
Hydroxylamine hydrochloride	Aldrich	Reagent-Plus	99%
3-Methyl-butynol	Aldrich		98%
Bauxite garandela	Alcan		
Bauxite amdoom	Alcan		

GC/MS analyses. GC/MS analyses were performed on a GC *Agilent 6890N* with a MSD *Agilent 5973N* equipped with a split injection system, an autosampler and auto-injector *Agilent7863* controlled by the MSD Productivity ChemStation software, and a HP-5MS capillary column (30m x 0.250mm x 0.25µm). The MSD uses an EI ionization mode with energy of 70 eV. Table 14 lists other GC/MS conditions. The products of aerobic oxidations of substrates were qualified by the software "NIST 02 Library" according to their MS spectra. A series of standard solutions containing substrates and their oxidation products were prepared to set up a calibration curve (concentration compared to chromatographic peak area) for

quantifying unknown samples. The concentration range of the calibration curve is from 1.84 x 10^{-4} to 0.003 mmol / mL. Since the maximum oven temperature is 320°C, substrates of very high boiling points (above 305°C) are analyzed by NMR only.

Table 14: GC/MS conditions

Part	Conditions					
Injector	Injector volume --	1 uL				
Inlet	Heater --	250°C or 10°C above the boiling point of substrates				
	Split ratio --	100:1				
	GasSaver --	20 mL/min@ 2 m			Gas --	Helium
Column	Mode --	Constant flow			Detector --	MSD
	He flow --	1 mL/min				
Oven	Initial temp. --	80°C			holding time --	0 min
	rate 1 --	20°C/min	next temp. --	135°C	holding time --	0 min
	rate 2 --	5°C/min	next temp. --	150°C	holding time --	1 min
	rate 3 --	15°C/min	next temp. --	300°C	holding time --	1 min
	Total running time --	17,75 min				
MSD	Heater --	280°C	Solvent Delay --	1,45 min	Acq. Mode --	Scan

2.2 Procedures for oxidation reactions and for the preparations of the derivatives and analogues of NHPI

Procedure A – Aerobic oxidation by $Co(OAc)_2$/NHPI in organic solvents. A three-necked, 100-mL round bottom flask equipped with a condenser was charged with a solution of the substrate (3 mmol in 5-10 mL of ethyl acetate or acetronitrile, generally 8 mL). To this solution was added NHPI (48.9 mg, 0.3 mmol, 10 mol% with respect to the substrates) and $Co(OAc)_2$ (3.7 mg, 0.5 mol% with respect to the substrate). Aerobic oxidations often were carried out at 60 °C.

The condenser was then fitted with a plastic balloon, which was filled with O_2 (1 atm). The reactions requiring air instead of oxygen were carried out in 50 mL flasks equipped with a condenser that was open at the top to laboratory air. The reaction mixture was stirred at the desired temperature for 20 h, unless otherwise indicated. The final reaction mixtures were then transferred into a 10 mL volumetric flask and the volume brought to 10 mL by addition of more solvent. For GC/MS tests, 1 mL aliquots of these stock solutions were transferred into another 10-mL volumetric flask and further diluted to 100 mL (1000 dilution times at the end). As for NMR tests, a small portion (0.2-1 mL) of the stock solution was evaporated to dryness, and then the solid or oil was dissolved in $CDCl_3$, C_6D_6, or DMSO-d_6 according to its polarity. A portion of hexamethyl benzene (3-5 mg) was added to the sample as an internal standard for quantifying the results.

Procedure B – Aerobic oxidation by $Co(OAc)_2$/NHPI in aqueous media. A three-necked, 100 mL round bottom flask equipped with a condenser was charged with aqueous media of the substrate (3 mmol). The condenser was then fitted with a plastic balloon, which was filled with 1 atm of O_2. To this solution was added NHPI (15 mol% based on the substrates) and $Co(OAc)_2$ (2 mol% with respect to the substrate), unless otherwise indicated. Generally aerobic oxidations were carried out in 8 mL of aqueous media at 60 °C for 20 h, unless otherwise mentioned. In addition when aqueous solutions were used without organic solvents miscible with water, 1 mol% of benzalkonium chloride was often applied in aerobic oxidations. Ethyl acetate was used to extract organics in the final aqueous mixtures, and then the organic phase was dried over $MgSO_4$. After filtration the organic phase was transferred into a 50 or 100-mL volumetric flask, and diluted to the mark.

Then, 0.5 or 1 mL of these stock solutions was transferred into another 10-mL volumetric flask for GC/MS tests (1000 dilution times at the end). A portion (0.2-1 mL) of the stock solution was evaporated to dryness for NMR tests. Hexamethyl benzene was employed as an internal standard for quantifying the results.

Procedure C – Aerobic oxidation by iron catalysts/NHPI in organic solvents. A procedure similar to **A** was followed. Ethyl acetate (8 mL) was used as solvent. Iron-based catalysts (generally 5 mol%) were used as co-catalysts instead of $Co(OAc)_2$ in aerobic oxidations catalyzed by NHPI (10 mol%) under 1 atm of dioxygen.

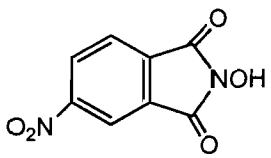
Procedure D – Aerobic oxidation by iron catalysts/NHPI in aqueous media. A procedure similar to **B** was followed. Aqueous media (8 mL) was used as solvent. Iron-based catalysts (10 mol%), $Fe(NO_3)_3{\cdot}9H_2O$ or Fe_2O_3, and NHPI (15 mol%) were used as catalysts.

Procedure E – Aerobic oxidation by $Co(OAc)_2$/4-nitro-NHPI in ethyl acetate. A procedure similar to **A** was followed. $Co(OAc)_2$ (0.5 mol%) and 4-nitro-NHPI (10 mol%) were used as catalysts.

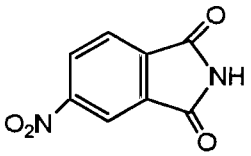
Procedure F – Aerobic oxidation by $Fe(NO_3)_3{\cdot}9H_2O$/4-nitro-NHPI in aqueous media. A procedure similar to **B** was followed. $Fe(NO_3)_3{\cdot}9H_2O$ (10 mol%) and 4-nitro-NHPI (15 mol%) were used as catalysts.

Procedure G – Preparation of 4-nitro-NHPI. According to the literature reports, there are two possible pathways of synthesis 4-nitro-NHPI: 1) from 4-nitrophthalimide[49] or 2) from 4-nitrophthalic anhydride[50] (in Figure 6).

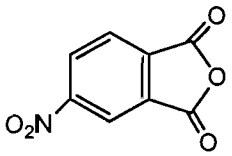
Figure 6: the strctures of 4-nitro-NHPI, 4-nitrophthalimide, and 4-nitrophthalic anhydride



4-nitro-NHPI



4-nitrophthalimide

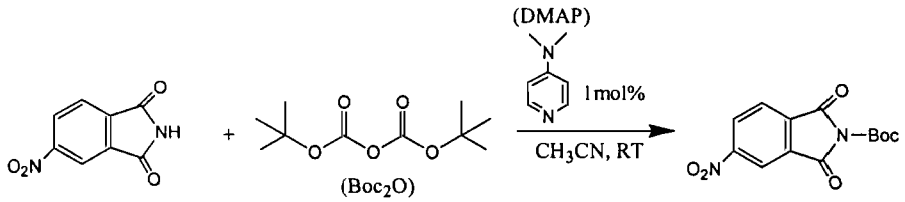


4-nitrophthalic anhydride

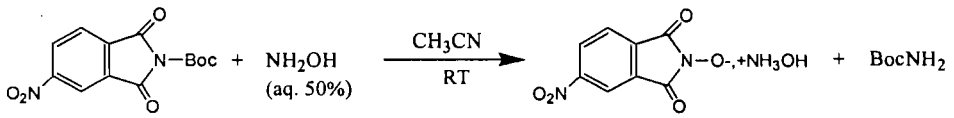
1) From 4-nitrophthalimide.[49] To a suspension of 4-nitrophthalimide (10 mmol, 1.96 g) in 20 mL of acetonitrile at room temperature was added di-*tert*-butyldicarbonate (1.5 eq. 3.38 g) followed by dimethylaminopyridine (DMAP) (10 mol%, 0.12 g). After 30 minutes, TLC (CH_2Cl_2: EtOAc = 9:1) was used to monitor the progress of the reaction. When no starting material remained, an aqueous solution of hydroxylamine (1.5 eq., 0.94 mL of a 50 wt% aqueous solution) was added. After stirring the mixture overnight at room temperature, addition of 10 mL of Et_2O led to the precipitation of most of the hydroxyl ammonium salt of the N-hydroxyimide. The orange solid was filtered, washed thoroughly with Et_2O and dried. 15 mL of dilute HCl solution was added to these solids, and the pH was adjusted to 1. The color of the solids turned from orange to pale yellow. Ethyl acetate was employed to extract 4-nitro-NHPI and the aqueous phase was saturated with NaCl. The combined organic extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure. After evaporation, pale yellow solids of 4-nitro-NHPI were obtained.

According to this procedure, 4-nitro-NHPI was synthesized in 60-70% yield (Eq. 28-30). It is worth noting that the volumė of acetonitrile is a very important parameter. If too little acetonitrile was used, the reaction of Eq. 28 was incom-

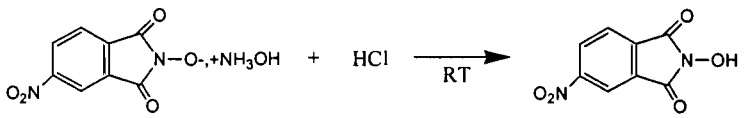
plete. If too much acetonitrile was used, the hydroxyl ammonium salts of the N-hydroxyimide could not be fully converted in the reaction of Eq. 29. Additionally, heating blocked the reaction of Eq. 28.



(Eq. 28)



(Eq. 29)



(Eq. 30)

Analytical parameters of 4-nitro-NHPI. Pale yellow crystals, yield 60-70%. ^{1}H NMR (400 MHz, δ, DMSO-d_6) 8.08 (d, 1H), 8.44 (s, 1H), 8.62 (d, 1H), 11.14 (s, 1H); ^{13}C {^{1}H} NMR (62.5 MHz, δ, DMSO-d_6) 119.0, 125.7, 130.9, 131.6, 135.1, 152.6, 163.6, 163.9.

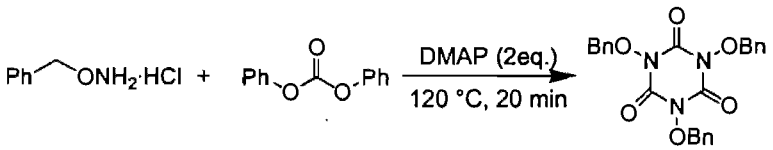
2) From 4-nitrophthalic anhydride. The synthesis from 4-nitrophthalic anhydride is based on the pathway introduced by Sugamoto and co-workers[50] from the reaction of phthalic anhydrides with hydroxylamine hydrochloride in the presence of pyridine under microwave irradiation. A mixture of 4-nitrophthalic anhydride (2 mmol, 420 mg), hydroxylamine hydrochloride (4 mmol, 281 mg), and pyridine (20 mmol, 1.62 mL) in a reactor tube was irradiated at 170°C in a Biotage® Initiator™ professional microwave heater (instead of an ordinary kitchen microwave oven) for 1 hour. The pyridine was removed under reduced pressure. The residue

was dissolved in methanol, and then this solution was transferred into a 25-mL volumetric flask for GC/MS tests. Unfortunately, this method did not work, and the product was 4-nitro-phthalimide rather than 4-nitro-NHPI.

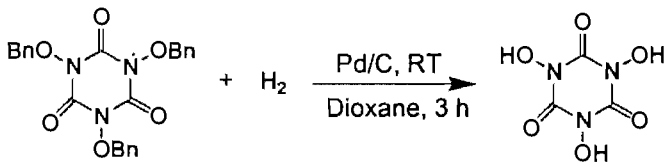
Procedure H – Preparation of THICA. A mixture of *o*-benzylhydroxylamine hydrochloride (1.61g, 10 mmol), diphenyl carbonate (2.16g, 10 mmol), and DMAP (2.47g, 20 mmol) was heated at 120 °C for 20 minutes. After cooling to room temperature, methanol (10 mL) was added to the reaction mixture and stirred for 20 minutes. The resulting precipitate was filtered off and washed with additional methanol (10 mL). The precipitate was dried under reduced pressure at 80 °C to give 1,3,5-tribenzyloxyisocyanurate. Then its hydrogenolysis on Pd / C (10% Pd, 0.25 g) was carried out in dioxane (50 mL) under normal pressure of H_2 at room temperature for 3 h. The catalyst was filtered off from the reaction mixture and washed with dried dioxane (10 mL). The filtrate was evaporated under reduced pressure to give THICA, as shown in Eq. 31-32.[51]

Unfortunately, the method did not work well, giving only a low yield. Although THICA is known as a more efficient radical-producing catalyst than NHPI, it was not used in our research because too little compounds were obtained.

Analytical parameters of THICA . White solids, yield ≤10%. ^{1}H NMR (400 MHz, δ, DMSO-d_6) 11.11 (s, 3H); ^{13}C {^{1}H} NMR (62.5 MHz, δ, DMSO-d_6) 146.9 (C=O).



(Eq. 31)



(Eq. 32)

Procedure I – Aerobic oxidation of humic acid sodium salt. A procedure similar to **B** was followed. The mixture of humic acid sodium salt (600 mg or 60 mg), cobalt acetate (14.9 mg), NHPI (73.4 mg), and benzalkonium chloride (10.5 mg) was heated in a 0.003 N NaOH solution at 80 °C for 20 h under 1 atm of dioxygen. Then the mixture was transferred into a 100-mL volumetric flask. The stock solution was diluted further for UV-vis tests.

Procedure J – Aerobic oxidation of the bauxite. A procedure similar to **B** was followed. A mixture of bauxite (Garandela, 600 mg), cobalt acetate (14.9 mg), and NHPI (73.4 mg) was heated in a 0.003 N NaOH solution at 80 °C for 20 h under 1 atm of dioxygen. After reaction the mixture was transferred into a 50-mL centrifuge tube, distilled water was added into the 40-mL mark. After centrifugation the upper clear solution or its dilute solution was used to do UV-vis tests.

Chapter 3: AEROBIC OXIDATIONS CATALYZED BY COMBINATIONS OF NHPI OR 4-NITRO-NHPI, AND TRANSITION METAL SALTS

This chapter discusses the results of oxidations catalyzed by combinations of transition metal salts and NHPI or 4-nitro-NHPI in a variety of conditions. The system of cobalt acetate and NHPI is well known as a highly effective catalyst for aerobic oxidation. Therefore, in organic solvents this system was evaluated first. We also studied the oxidative efficiency of iron salts because bauxite contains significant amounts of iron, raising the possibility of doing oxidations without the addition of metal salts. Meanwhile, because our ultimate goal is to carry out the oxidation reactions in aqueous media and since the fragment of "-NO_2" in 4-nitro-NHPI is thought to increase its water solubility, the influence of 4-nitro-NHPI on oxidation was also determined, especially in aqueous media. It should be noted that the catalyst loadings, the conversion, and the yields (mol%) are based on the amount of starting substrates used. Generally, the conversion and/or yield are determined by GC/MS tests, unless otherwise noted. The yields of some of the products were not determined by GC/MS tests because they were not identified or the samples of these species were not available at that time. The oxidized products were identified based on their MS spectra by using the software "NIST 02 Library".

3.1 Aerobic oxidations catalyzed by $Co(OAc)_2$/NHPI

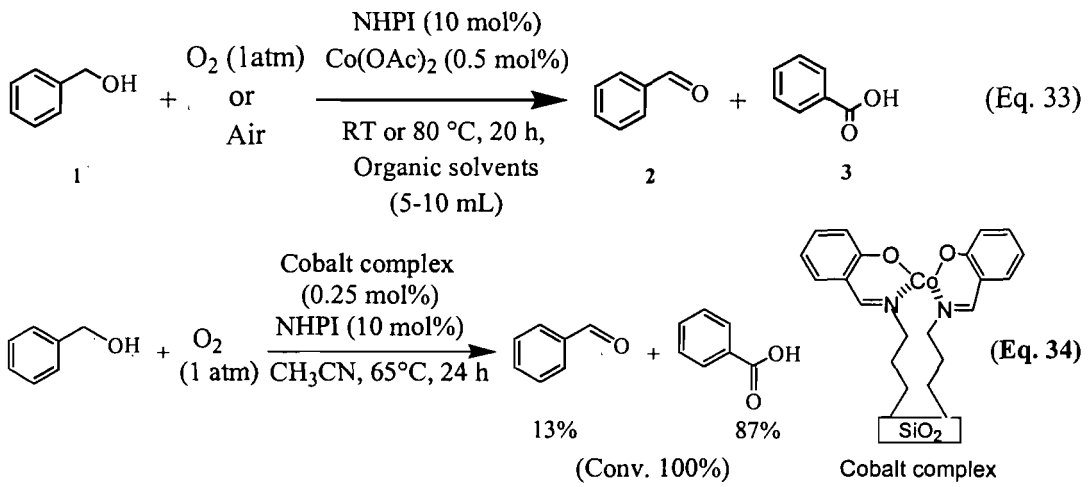
3.1.1 Aerobic oxidation in organic solvents

According to Procedure **A**, these oxidation reactions were carried out for 20 h in organic solvents (EtOAc or CH_3CN) in the presence of the catalytic system consisting of 0.5 mol% of cobalt acetate and 10 mol% of NHPI under 1 atm of dioxygen or in air. In some reactions, *m*-chlorobenzoic acid (MCBA), which is thought to facilitate the decomposition of in-situ produced alkylhydroperoxides, was used to evaluate its influence on aerobic oxidation. All test results are listed in Table 15.

3.1.1.1 Oxidation of benzyl alcohol

As shown in Eq. 33, benzylalcohol was converted into benzaldehyde (**2**) and benzoic acid (**3**). Aerobic oxidations of benzyl alcohol proceeded readily such that even at room temperature and using air we obtained ca. 50% conversion (Run 1-1). Moreover, with the addition of MCBA, the oxidative efficiency went down a little (Run 1-1 and Run 1-2). With the increase of temperature, the conversion of benzyl alcohol rose to ca. 70-100 % (Run 1-3 to 1-5). Using oxygen resulted in complete conversion to benzoic acid at room temperature (Run 1-7). The influence of various organic solvents was also determined as follows: AcOH > CH_3CN > EtOAc > PhCN (from Run 1-3 to Run 1-6). Although AcOH is the best solvent, EtOAc and/or CH_3CN were chosen in most of aerobic oxidations because AcOH is harmful to GC column and it is expensive. F. Rajabi and B. Karimi also reported[40] that benzyl alcohol was oxidized into benzoic acid with 87% yield by the catalytic

system of a recyclable heterogeneous cobalt acetate and NHPI under 1 atm of dioxygen at 65 °C (Eq. 34). In comparison, our system of $Co(OAc)_2$ and NHPI worked better than the one of NHPI and the heterogeneous cobalt complex although a little more $Co(OAc)_2$ (0.5 mol%) was used by us, and in our studies benzyl alcohol was fully oxidized into benzoic acid at room temperature in CH_3CN (Run 1-7).



3.1.1.2 Oxidation of styrene

Styrene was catalytically oxidized to mainly benzaldehyde (**2**) and 2-phenyl-oxirane (**6**) with low conversion under air at 80 °C (Run 2-1). MCBA did not have any positive influence on aerobic oxidation of styrene; indeed, the presence of MCBA led to a small decrease in the oxidative efficiency (Run 2-1 and Run 2-2). The conversion improved when the reaction was carried out under 1 atm of O_2 at 60 °C, but this approach also generated many by-products, including benzaldehyde (**2**), diphenylethanedione (**5**), benzoic acid (**3**), and 2-phenyl-oxirane (**6**), and other minor products not exceeding 1% (as estimated from their peak areas), as shown in

Table 15: Aerobic oxidations of various substrates in organic solvents catalyzed by $Co(OAc)_2$ / NHPI under 1 atm of air or O_2

Run	Substrates	Temp. (°C)	Sovlent	Additives	Air or O_2	Appearance	Conv. (mol%)	Yield of oxidized product (mol%)			
1-1	Benzyl alcohol (*1*)	22	EtOAc (8 mL)	--	Air	Yellow cloudy	48%	***2*** (43%)	***3*** (5%)		
1-2		22	EtOAc (8 mL)	MCBA (5%)	Air	Yellow cloudy	42%	***2*** (38%)	***3*** (5%)		
1-3[*a]		80	EtOAc (5 mL)	--	Air	Green	71%	***2*** (46%)	***3*** (25%)		
1-4[*a]		80	CH_3CN (5 mL)	--	Air	Green	92%	***2*** (35%)	***3*** (57%)		
1-5[*a]		80	AcOH (5 mL)	--	Air	Light green	100%	***2*** (6%)	***3*** (94%)		
1-6[*a]		80	PhCN (5 mL)	--	Air	Dark yellow	58%	***2*** (41%)	***3*** (17%)		
1-7		21-22	CH_3CN (10 mL)	--	O_2	Green	100%	***2*** (trace)	***3*** (>99%)		
2-1	Styrene (*4*)	80	EtOAc (8 mL)	--	Air	Pale yellow cloudy	28%	***2*** (9%)	***6*** (8%[*b])		
2-2		80	EtOAc (8 mL)	MCBA (5%)	Air	Green clear	22%	***2*** (8%)	***6*** (5%[*b])		
2-3		60	EtOAc (8 mL)	--	O_2	Yellow cloudy	52%	***2*** (12%)	***5*** (5%[*b])	***6*** (2%[*b])	***3*** (2%[*b])
3-1	Toluene (*9*)	80	EtOAc (8 mL)	--	Air	Yellow cloudy	27%	***2*** (2%)	***3*** (13%)		

Run	Substrates	Temp. (°C)	Sovlent	Additives	Air or O_2	Appearance	Conv. (mol%)	Yield of oxidized product (mol%)			
3-2	Toluene (*9*)	80	EtOAc (8 mL)	MCBA (5%)	Air	Green clear	25%	*2* (2%)	*3* (13%)		
3-3		18-22	EtOAc (8 mL)	--	O_2	Orange cloudy	15%	*2* (0.6%)			
3-4		60	EtOAc (8 mL)	--	O_2	Yellow, cloudy	63%	*2* (1%)	*3* (54%)		
4-1	Cumene (*10*)	22	CH_3CN (10 mL)		O_2	Yellow, cloudy	9%[*a]	*11* trace	*12* trace	*13*[*b] (4%)	
4-2		60	CH_3CN (8 mL)	--	O_2	Light orange cloudy	99%	*11* (51%)	*12* (20%)	*13*[*b] (≤30%)	
4-3		60	EtOAc (8 mL)	--	O_2	Yellow cloudy	92%	*11* (49%)	*12* (18%)	*13*[*b] (≤30%)	
4-4		60	EtOAc (8 mL)	Ac_2O (10%)	O_2	Olive green cloudy	33%	*11* (12%)	*12* (10%)	*13* (trace)	
5-1[*a]	Indane (*14*)	52-60	EtOAc (8 mL)	--	O_2	Yellow cloudy	100%	*15* (85%)			
5-2		23	CH_3CN (10 mL)	--	O_2	Yellow	95%	--			
6[*a]	Indene (*16*)	60	EtOAc (8 mL)	--	O_2	Orange cloudy	99%	See Table 23			
7	*p*-Xylene (*19*)	60	EtOAc (8 mL)	--	O_2	Green, cloudy, white precipitate	79%	*20* (2%[*a])	*21* (59%[*a])	*22* (trace)	*23* (4%[*a])
8[*a]	Fluorene (*24*)	60-72	EtOAc (8 mL)	--	O_2	Orange cloudy	45%	*25* (44%)			

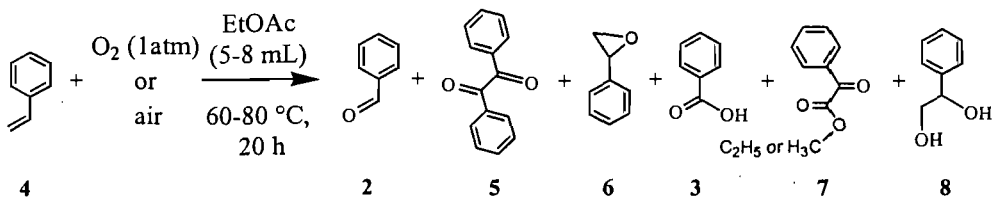
Run	Substrates	Temp. (°C)	Sovlent	Additives	Air or O_2	Appearance	Conv. (mol%)	Yield of oxidized product (mol%)			
9	Xanthene (*26*)	60-72	EtOAc (8 mL)	--	O_2	Orange cloudy	96%[*a]	*27* (62%[*a])	*28* (≅14%[*b])	*29* (≅1%[*b])	*30* (trace)
10	Isochroman (*31*)	60	EtOAc (8 mL)	--	O_2	Yellow cloudy	100%	*32* (≥99%)			
11	2-Phenyl-2-propanol (*11*)	80	EtOAc (8 mL)	--	O_2	Brown	0%	--			
12	*trans*-Cinnamic acid (*33*)	80	EtOAc (8 mL)	--	O_2	Brown	0%	--			
13-1	Chromone (*34*)	60	EtOAc (8 mL)	--	O_2	Brown cloudy	0%	--			
13-2[*d]		100	EtOAc (8 mL)	--	O_2	Brown cloudy	0%	--			
14-1	Benzyl amine (*35*)	80	EtOAc (5 mL)	--	Air	Brown	0%	--			
14-2		80	EtOAc (5 mL)	Benzyl alcohol (*1*) (100%)	Air	Brown	0%	Benzyl alcohol didn't be oxidized			

*[a] Based on NMR tests.

*[b] The data were estimated from the peak area in the GC/MS spectra because their samples were not available at that time.

*[c] 1 mol% of cobalt acetate and 20 mol% of NHPI were use

Eq. 35. Table 16 lists the compounds corresponding to the peaks in the GC spectrum of oxidation of styrene in Run 2-3 (Figure 7). It is noted that phthalimide (RT=7.16 min) was the decomposition product of NHPI rather than the oxidized product of styrene, and the unknown compound (RT=15.67 min) likely arose from the reaction of NHPI and its structure could not be identified from the MS spectrum (Figure 8).



4 2 5 6 3 7 8 **(Eq. 35)**

Table 16: Peaks in GC spectrum of styrene oxidation for Run 2-3 (Figure 7)

No.	Retention time (min)	Compound name	Compound No.
1	2.10	Styrene	4
2	2.43	Benzaldehyde	2
3	3.03	2-Phenyl-oxirane	6
4	3.06	Diphenylethanedione	5
5	3.59	Benzoic acid	3
6	4.42	Oxo-phenyl-acetic acid methyl ester or Oxo-phenyl-acetic acid ethyl ester	7
7	5.02	1-Phenyl-ethane-1,2-diol	8
8	7.16	Phthalimide	--
9	15.67	Unknown	--

Figure 7: GC spectrum of styrene oxidation for Run 2-3

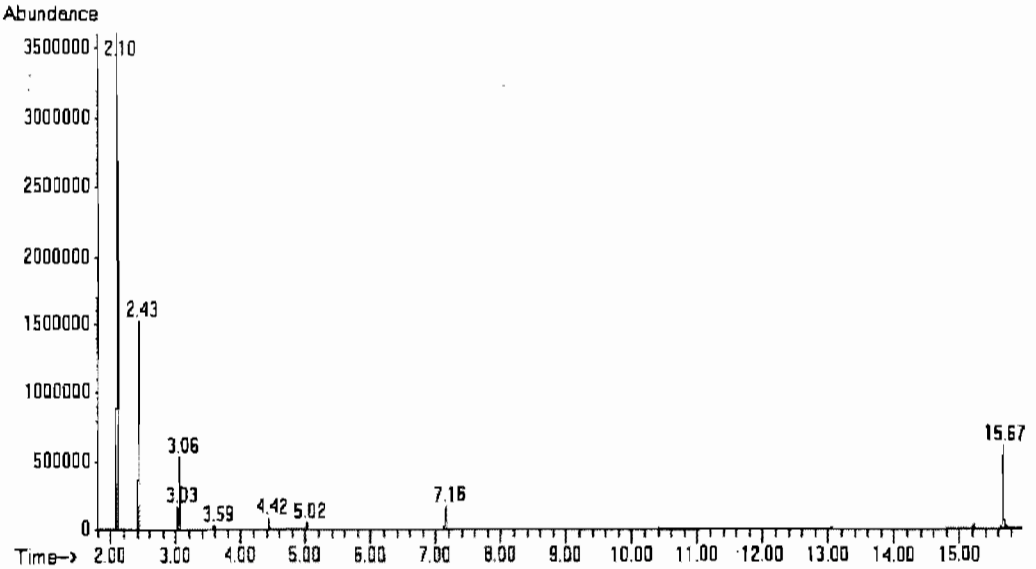
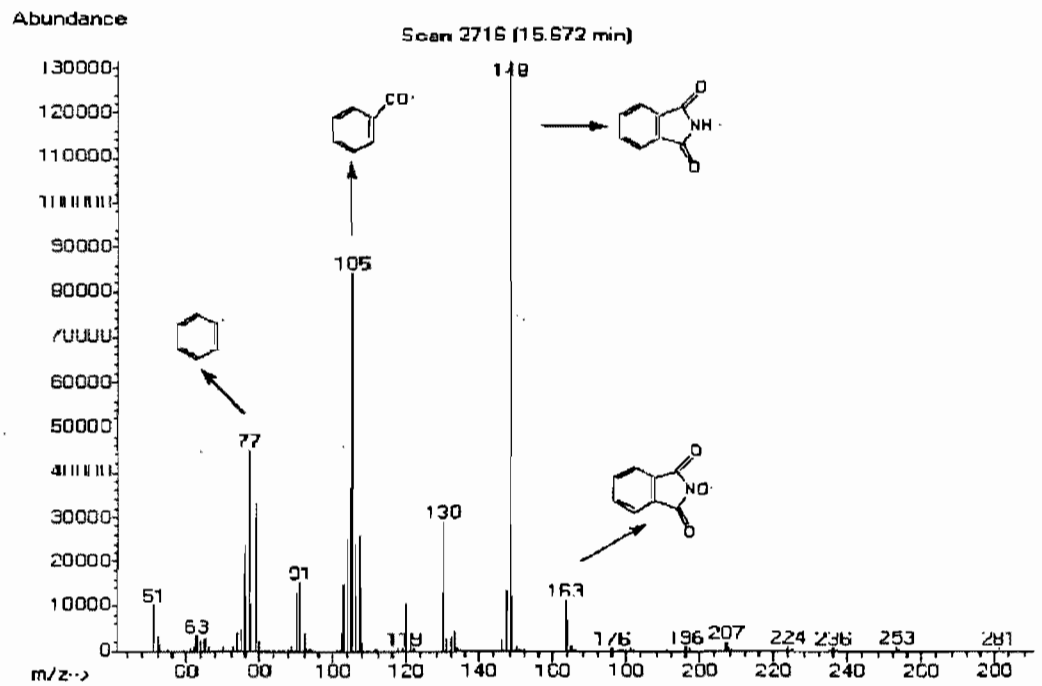
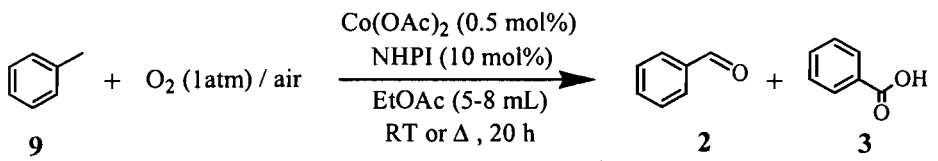


Figure 8: MS spectrum of the unknown product at RT=15.67 min of styrene oxidation (Run 2-3)

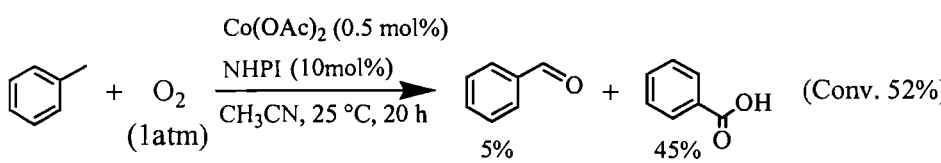


3.1.1.3 Oxidation of toluene

As shown in Eq. 36, toluene was converted mainly into benzaldehyde (**2**) and benzoic acid (**3**) with a fair conversion (27%) at 80 °C under air. The rate of oxidation was decreased a little in the presence of MCBA (run 3-1 and 3-2). Conducting the reaction under 1 atm of oxygen and at room temperature, gave a low conversion (15% conv., Run 3-3), but heating to 60 °C gave the best result (63% conv., Run 3-4). In our studies, the system of $Co(OAc)_2$ and NHPI did not work so well on aerobic oxidation of toluene, compared to Ishii's reports[35] in which toluene was oxidized with a 52% conversion in CH_3CN at 25 °C (Eq. 37). The discrepancy between these results is possibly due to the use of CH_3CN in Ishii's method.



(Eq. 36)

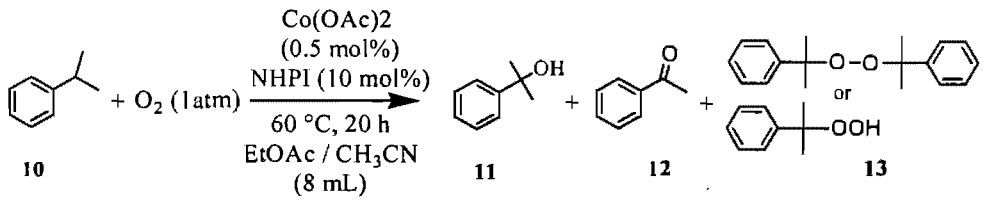


(Conv. 52%) (Eq. 37)

3.1.1.4 Oxidation of cumene

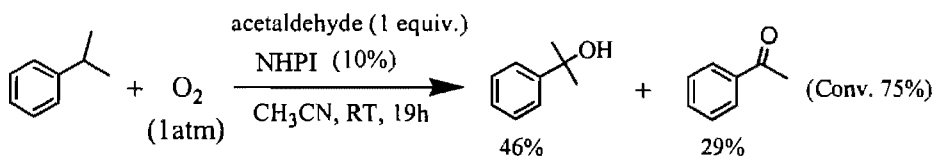
Aerobic oxidation of cumene in organic solvents. As show in Eq. 38, cumene was converted into 2-phenyl-2-propanol (**11**), acetophenone (**12**), and dicumyl peroxide or cumene hydroperoxide (**13**) with a very good conversion under 1 atm of oxygen at 60 °C (Run 4-2 and 4-3) although a little cumene was oxidized at RT (Run 4-1). The main product of these reactions was 2-phenyl-2-propanol (**11**). We also obtained variable amounts of a secondary product identified as either cumene hydroperoxide or dicumyl peroxide (compound **13**). The yield of this

product varied from traces to about 30% and could not be quantified accurately because this product appeared to be unstable, decomposing readily.



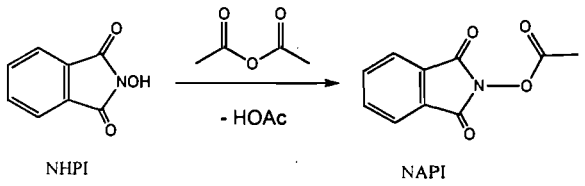
(Eq. 38)

Comparing our results (Run 4-3) to Einhorn's work (Eq. 39)[48], aerobic oxidation of cumene catalyzed by $Co(OAc)_2$/NHPI proceeded better with a 99% conversion although heating was needed. Moreover, in Einhorn's work, a large amount of co-catalyst, acetaldehyde (1 equiv.), was used so that a lot of organics were introduced in the system and conflicted with our objective to decrease organics. Meanwhile, the addition of acetaldehyde required using a syringe pump so as to complicate the process.



(Eq. 39)

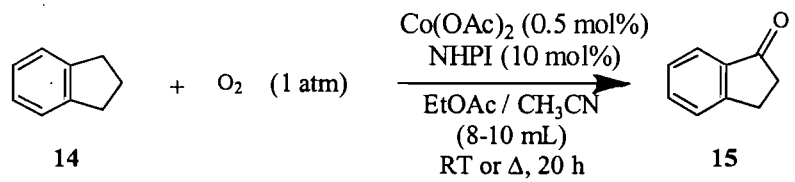
Influence of Ac_2O on aerobic oxidation of cumene. NHPI undergoes gradual decomposition under aerobic oxidation conditions, which compromises its oxidative efficacy. Ishii and co-workers have suggested that NAPI could be a better catalyst because it is more resistant to decomposition. NAPI is easily prepared by the reaction of NHPI with acetic anhydride (Ac_2O) (Eq. 25).[41] Therefore, the influence of Ac_2O was tested in aerobic oxidations (Run 4-4). Our experiments show that Ac_2O has a negative influence on the oxidative efficiency of the system of $Co(OAc)_2$/NHPI/O_2.



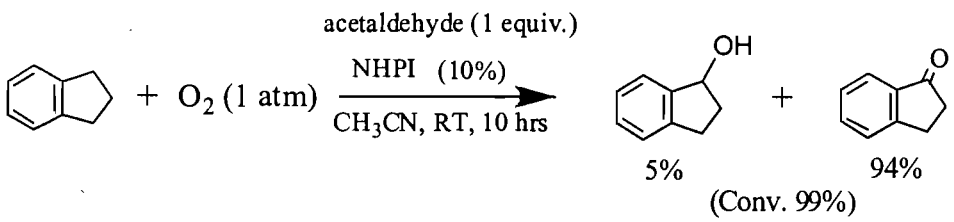
(Eq. 25)

3.1.1.5 Oxidation of indane

As shown in Eq. 40, indane was oxidized to 1-indanone in EtOAc with a 85% yield under 1 atm of oxygen at ca. 60 °C (Run 5-1). The reaction also proceeded at room temperature in CH_3CN with a very good conversion (95% conv., Run 5-2). Einhorn and co-workers also reported[48] that indane was oxidized by the system of NHPI and acetaldehyde with a 99% conversion (Eq. 41). Although the system of NHPI/acetaldehyde had a similar influence on aerobic oxidation of indane with our system of $Co(OAc)_2$/NHPI, the use of acetaldehyde complicated the process and introduced much organics into the reaction mixture.



(Eq. 40)



(Eq. 41)

3.1.1.6 Oxidation of indene

As shown in Eq. 42, indene was oxidized readily to a number of products including 2-indanone (**17**) and 2-methyl-benzaldehyde (**18**), plus variable amounts of phthalide, coumarin, 2-formyl-benzoic acid, benzenedicarboxaldehyde, etc. Ta-

ble 17 lists the possible compounds corresponding to the peaks in the GC spectrum (Figure 9), but some peaks cannot be estimated from their MS spectra (Figure10). Indane (RT=2.94 min) and 3,5-dimethyl ethyl benzene (RT=3.03 min) were impurities present in the starting substrate– indene. 1-Indanone (RT=5.00 min) was likely the oxidized product of indane oxidation. Phthalimide (RT=7.34 min) was the decomposed product of NHPI. 1,2-Benzenedicarboxylic acid (or phthalic anhydride, RT= 5.38 min) is also produced from decomposition of NHPI or generated from the further oxidation of 1,2-benzenedicarboxaldehyde (RT= 4.58), which is the product of indene oxidation. Because the peak of indene partly overlapped with other peaks and it was very small in the GC/MS spectrum of indene oxidation, indene could not be quantified by the GC/MS spectrum. Therefore, the quantification of indene was based on NMR tests.

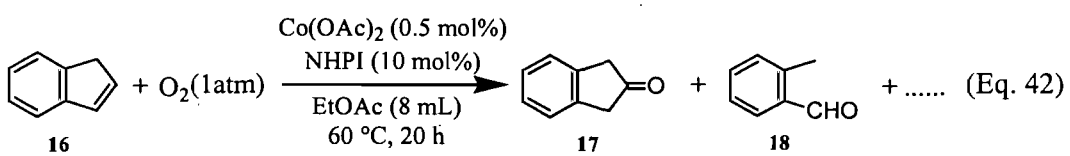


Figure 9: GC spectrum of indene oxidation

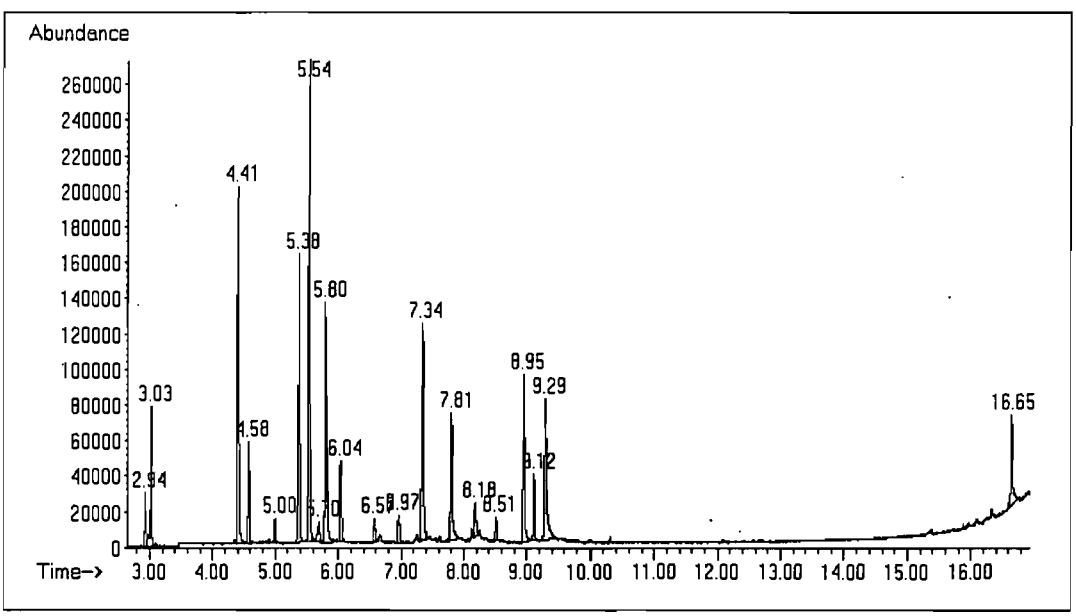
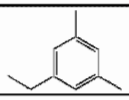
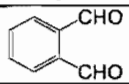
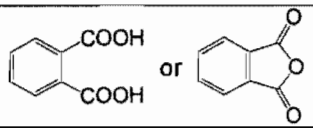
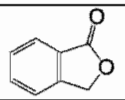
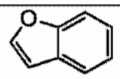
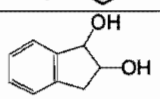
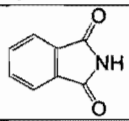
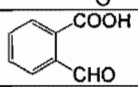
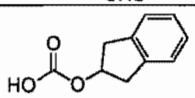
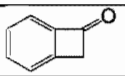
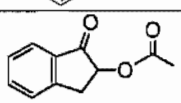
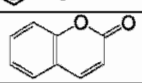
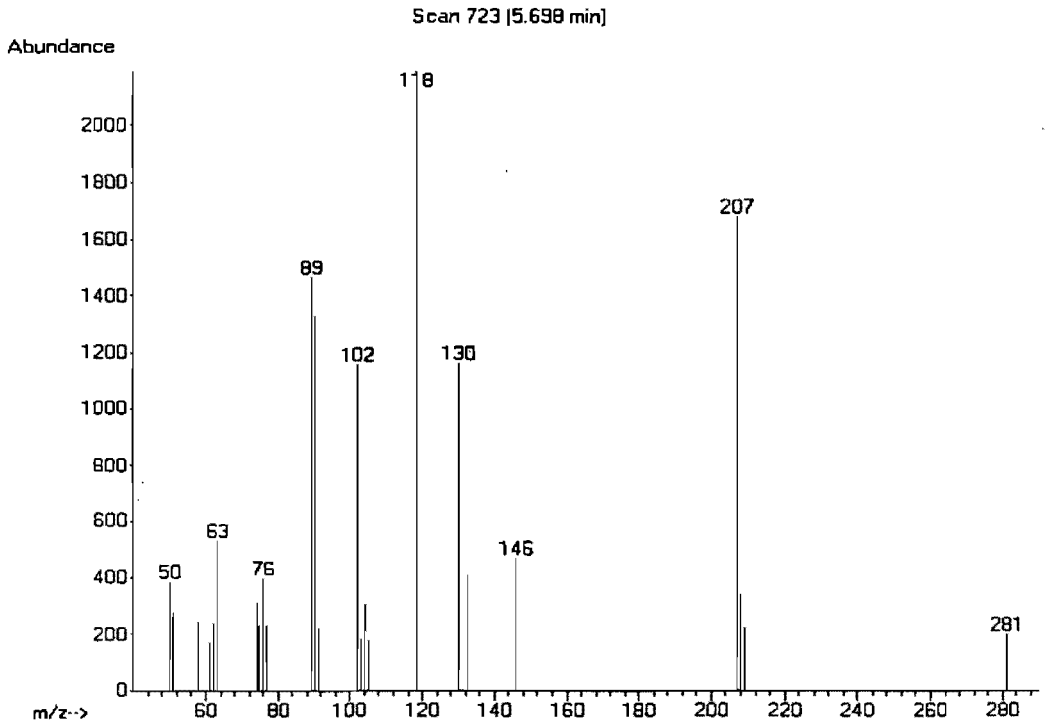


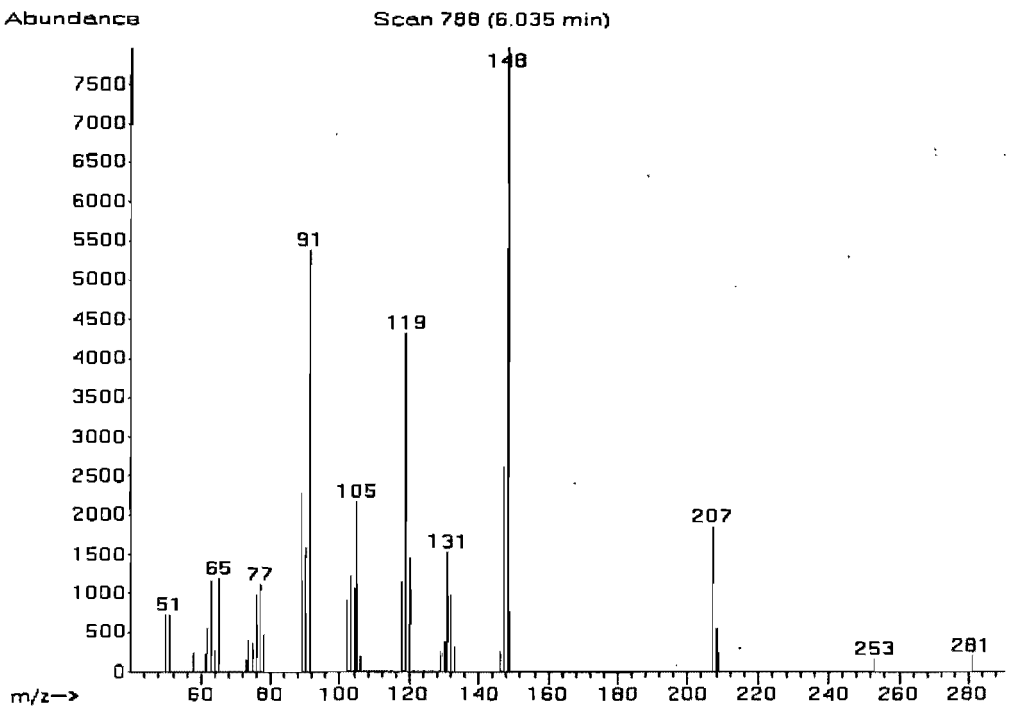
Table 17: Peaks in the GC spectrum of indene oxidation (Figure 9)

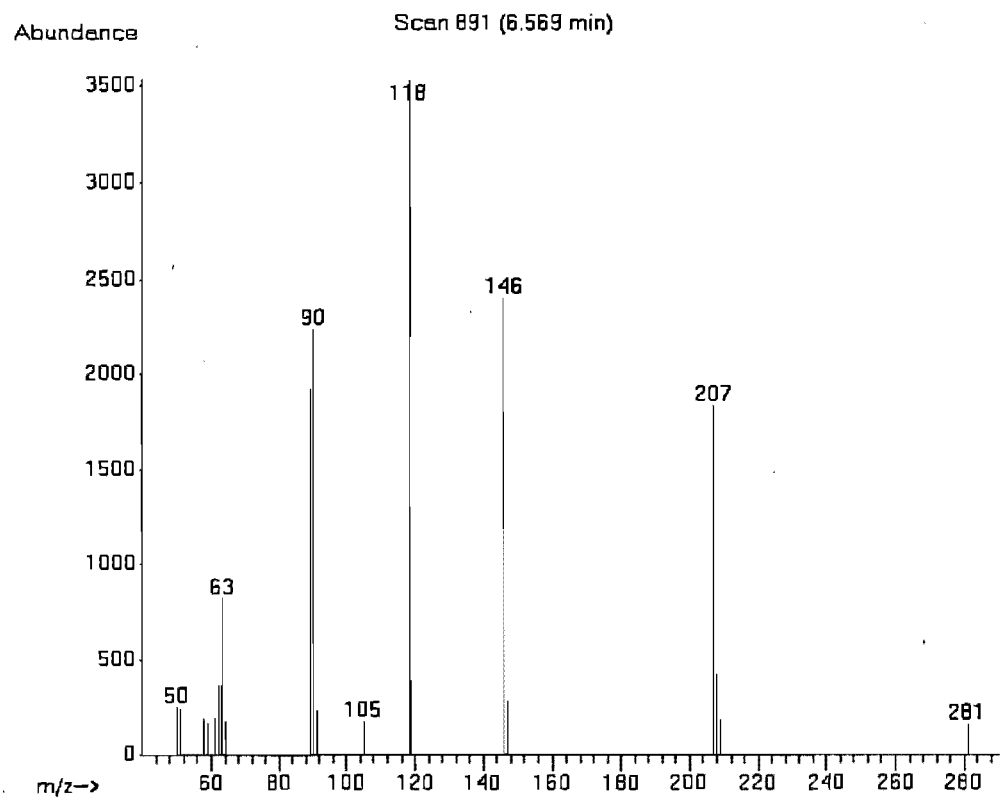
No.	Retention time (min)	Compound name	Compound No. or structure	Yield (mol%)[*1]
1	2.94	Indane	**14**	--
2[*2]	3.03	3,5-Dimethyl ethylbenzene		--
3	4.41	2-Indanone	**17**	13.1
4	4.58	Benzenedicarboxaldehyde		3.7
5	5.00	1-Indanone	**15**	--
.6	5.38	1,2-Benzenedicarboxylic acid or phthalic anhydride		12.3
7	5.54	2-Methyl-benzaldehyde	**18**	20.5
8[*3]	5.70	Unknown	--	1.4
9	5.80	Phthalide		12
10[*3]	6.04	Unknown	--	4.0
11[*4]	6.57	Benzofuran		1.3
12	6.97	1,2-Diol-2,3-dihydro-1H-indene		1.5
13	7.34	Phthalimide		--
14	7.81	2-Formyl benzoic acid		7.0
15[*4]	8.18	2-Indanylcarbonate, or Carbonic acid, mono-indan-2-yl ester		1.9
16[*3]	8.51	Unknown	--	1.2
17	8.95	Benzocyclobutenone		7.8
18[*2]	9.12	1-Oxo-indan-2-ylacetate or Acetic acid, 1-oxo-indan-2-yl ester		2.8
19	9.29	Coumarin		9.7
20[*5]	16.65	Decamethyltetrasiloxane	--	--

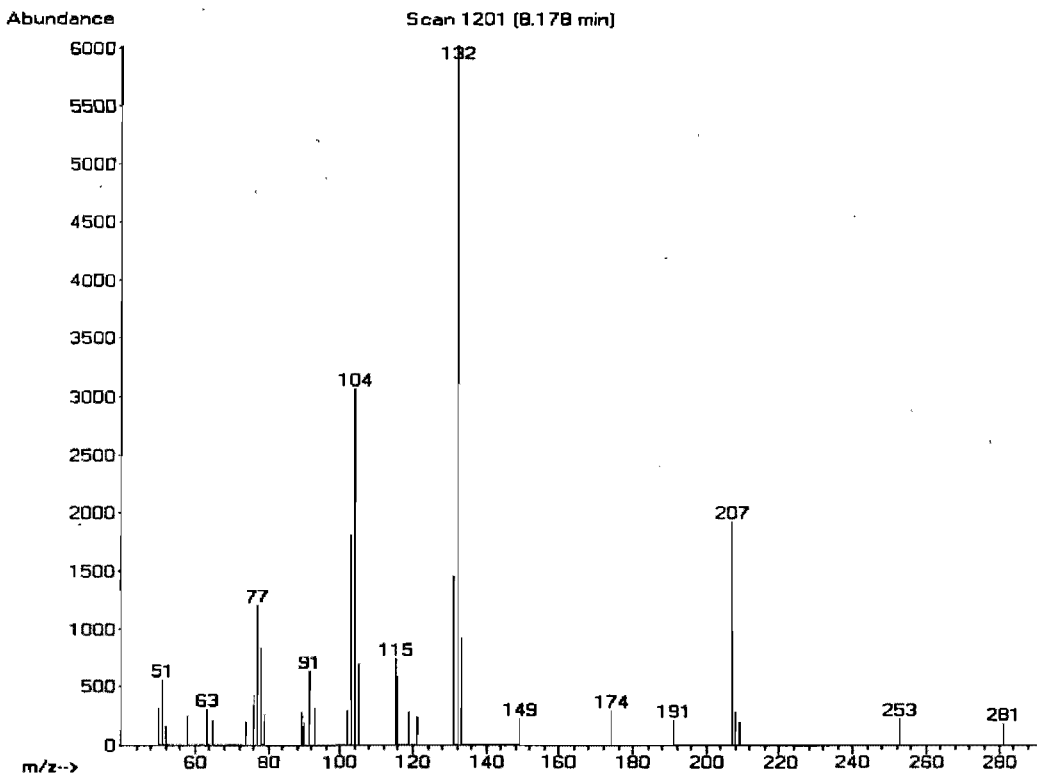
[*1] The yields were estimated from the peak areas in the GC traces. [*2] 3,5-Dimethyl ethylbenzene is an impurity present in indene. [*3] These compounds are possible products suggested by the software "NIST 02 library", based on their MS spectra (Figure 10). The level of accuracy is lower than 70%. [*4] These structures could not be established by the software "NIST 02 library". [*5] This compound (RT= 16.65) containing the atom of Si, is likely from the GC column.

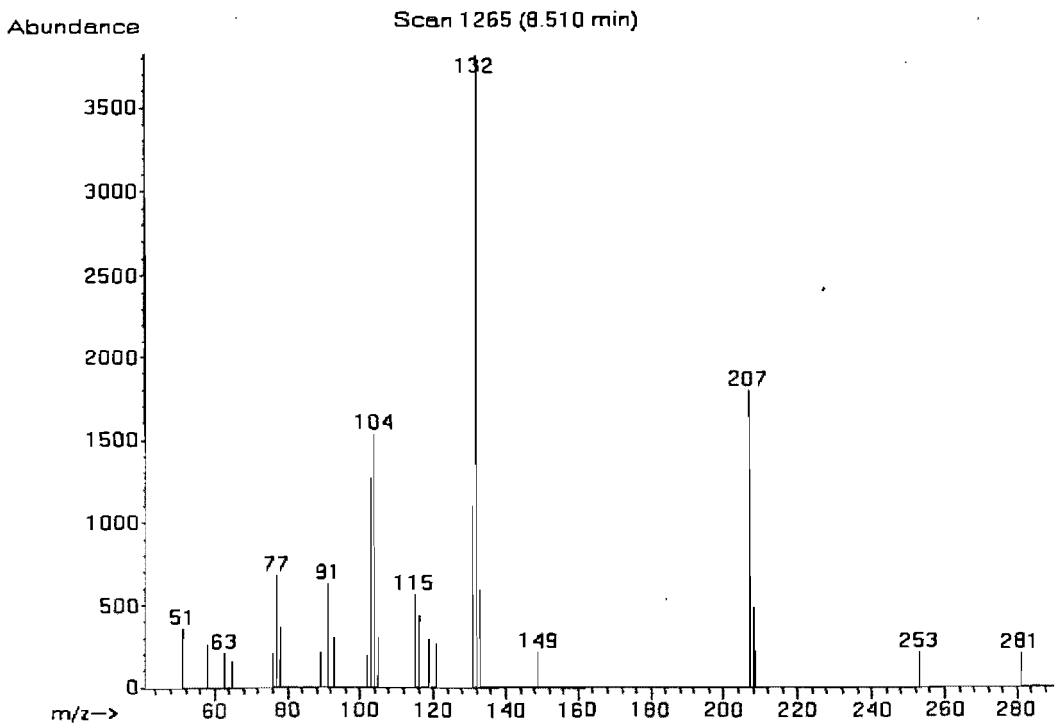
Figure 10: Some MS spectra of oxidized products of indene oxidation

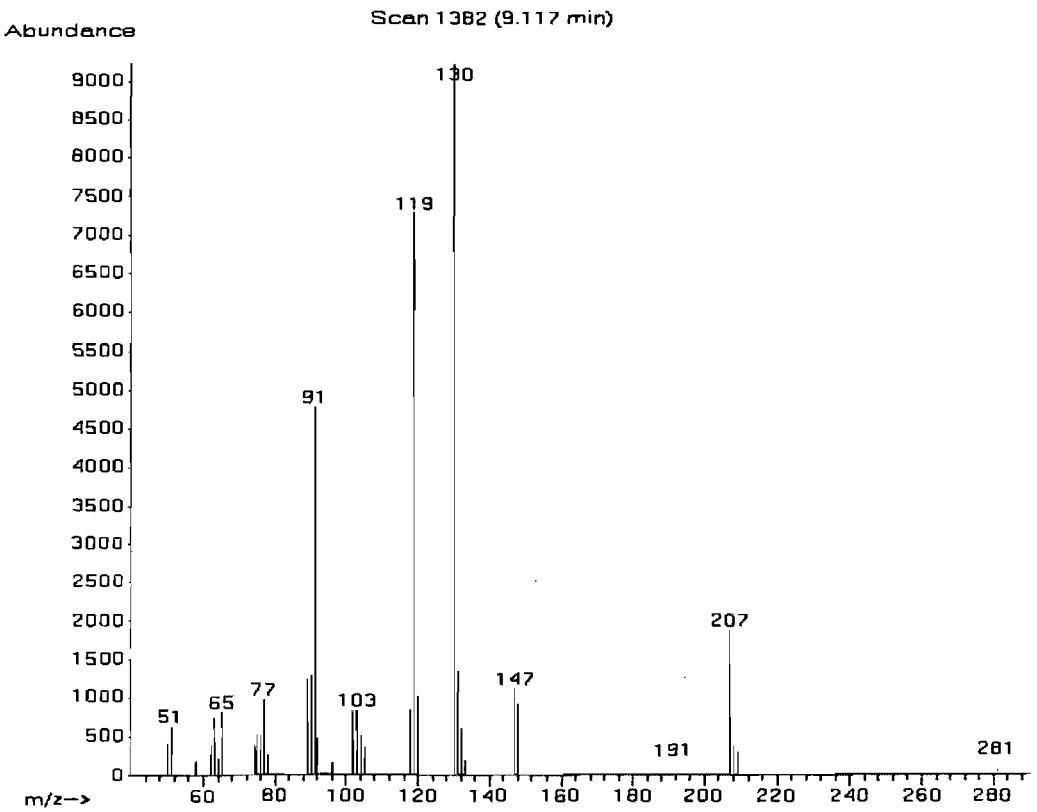





Abundance
Scan 891 (6.569 min)
3500
3000
2500
2000
1500
1000
500
0
118
146
90
207
63
50
105
281
m/z-->
60
80
100
120
140
160
180
200
220
240
260
280

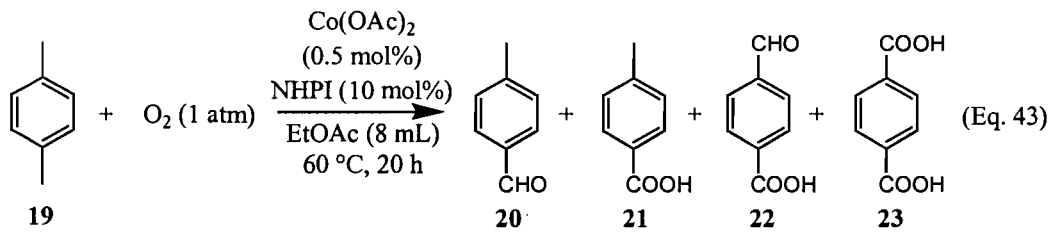

Abundance
Scan 1201 (8.178 min)
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
132
104
207
77
115
91
51
63
149
174
191
253
281
m/z-->
60
80
100
120
140
160
180
200
220
240
260
280


Abundance
Scan 1265 (8.510 min)
132
207
104
77
91
115
51
63
149
253
281
m/z->
3500
3000
2500
2000
1500
1000
500
0
60
80
100
120
140
160
180
200
220
240
260
280

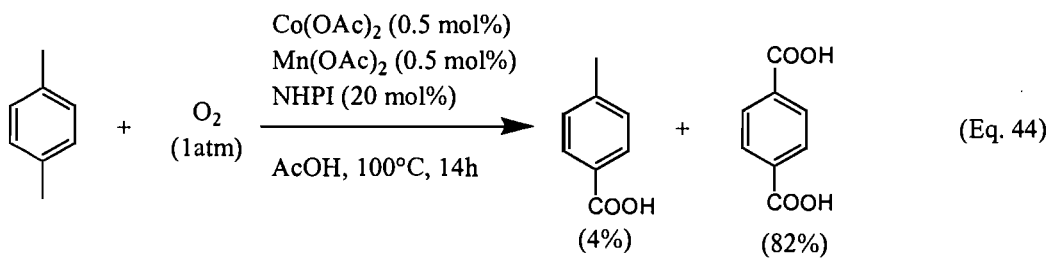

Abundance
Scan 1382 (9.117 min)
130
119
91
207
147
77
65
103
51
191
281
m/z->
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
60
80
100
120
140
160
180
200
220
240
260
280

3.1.1.7 Oxidation of *p*-xylene

p-Xylene was mainly converted into *p*-toluic acid (**21**) in a good yield (79%) under 1 atm of oxygen at 60 °C (Run 7). Other minor products were terephthalic acid (**23**), 4-methyl-benzaldehyde (**20**), and *p*-phthaldehydric acid (**22**), as shown in Eq. 43. *p*-Toluic acid was only sparingly soluble in ethyl acetate and precipitated as a white solid. The yields were determined by NMR using DMSO-d_6 as the solvent because of high polarity of the oxidized products of *p*-xylene oxidation. Hydroquinone was used as the internal standard for quantification. According to Tashiro's report,[42] the further oxidized product of *p*-xylene, terephthalic acid (**23**), was obtained in 82% yield at high temperatures when $Mn(OAc)_2$ was used in conjunction with $Co(OAc)_2$ and 20% NHPI, and the oxidation was carried out in AcOH instead of EtOAc (Eq. 44).



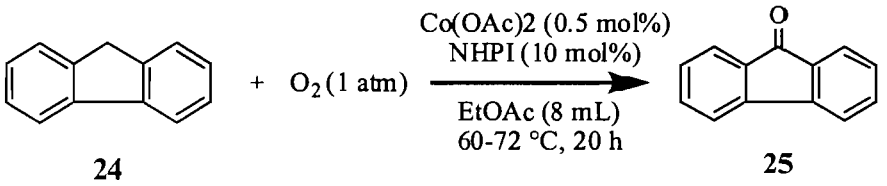
(Eq. 43)



(Eq. 44)

3.1.1.8 Oxidation of fluorene

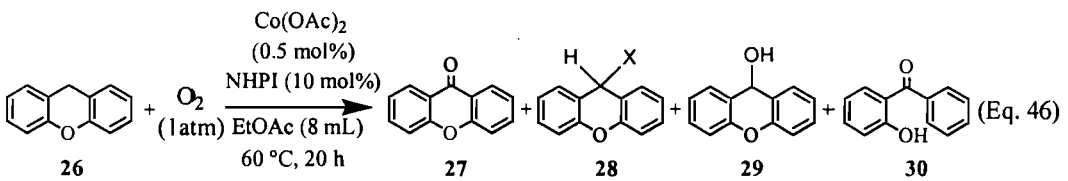
Fluorene was oxidized to 9-fluorenone under 1 atm of O_2 at ca. 70 °C in 45% conversion (Run 8, Eq. 45).



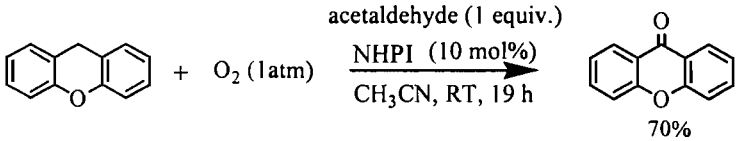
24 25 (Eq. 45)

3.1.1.9 Oxidation of xanthene

Xanthene was catalytically oxidized with 96% conversion under 1 atm of oxygen at 60 °C (Run 9). As shown in Eq. 46, the main products were xanthone (**27**), which was only sparingly soluble in ethyl acetate and precipitated as a white solid, and compound **28**; other minor oxidized products were 9-xanthenol (**29**) and 2-hydroxy-benzophenone (**30**). The structure of compound **28** (RT=17.72 min) is unknown, but it is estimated that the "X" group is likely "-OOH" (Figure 11). Einhorn and co-workers also reported[48] that xanthene was oxidized by the catalytic system of acetaldehyde and NHPI in a good conversion (94%) at room temperature (Eq. 47), but this method also had two drawbacks: using too much acetaldehyde and requiring more complex system.

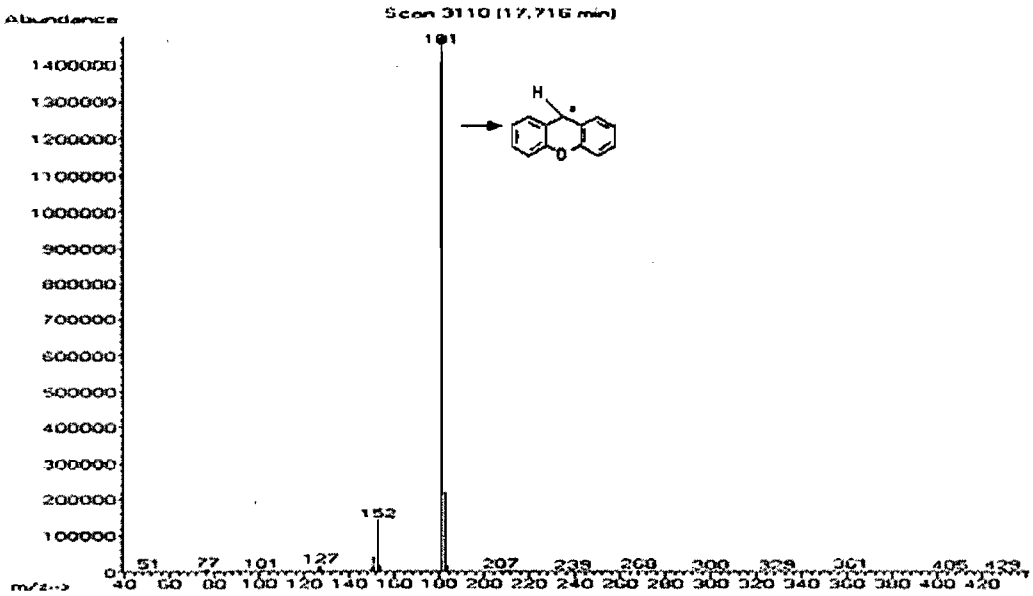


26 27 28 29 30 (Eq. 46)



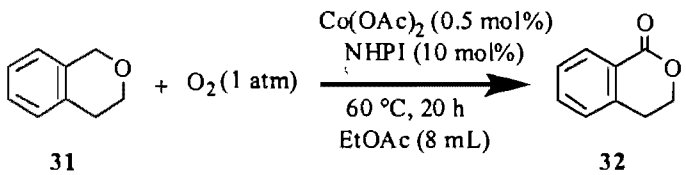
(Conv. 94%) (Eq. 47)

Figure 11: MS spectrum of the oxidized product 28 of xanthene oxidation

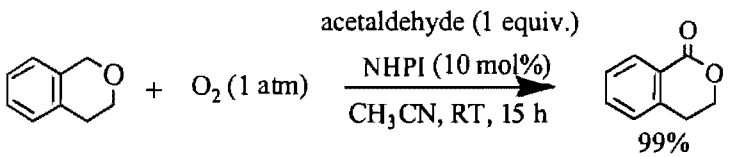


3.1.1.10 Oxidation of isochroman

Isochroman was oxidized with 100% conversion into 1-isochromanone (**32**) at 60 °C (Run 10, Eq. 48). Einhorn and co-workers also reported[48] that isochroman was fully oxidized by the catalytic system of acetaldehyde and NHPI at room temperature (Eq. 49). Compared to Einhorn's method, our system required heating, but it did not need to use a lot of acetaldehyde and the process was very simple.



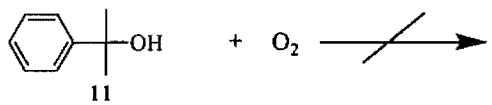
(Eq. 48)



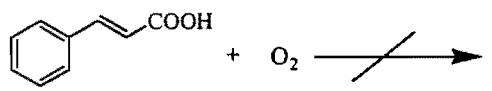
(Conv.100%) (Eq. 49)

3.1.1.11 Oxidation of 2-phenyl-2-propanol, *trans*-cinnamic acid, and chromone

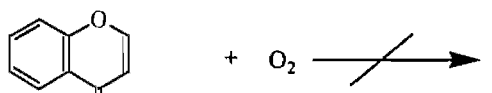
As shown in Eq. 50-52, 2-phenyl-2-propanol and *trans*-cinnamic acid could not be oxidized under 1 atm of oxygen at 80°C (Run 11-12), while chromone was also not oxidized under 1 atm of oxygen (Run 13) even at high temperature (100 °C) or by using high concentrations of catalysts ($Co(OAc)_2$ 1 mol%, NHPI 20 mol%). It is estimated that the absence of benzylic protons prevents the PINO radical generated from NHPI from abstracting a proton from α-carbon position of substrates and generating alkyl radicals so that the radical oxidation can not go on and no oxidation happens.



11 (Eq. 50)



33 (Eq. 51)

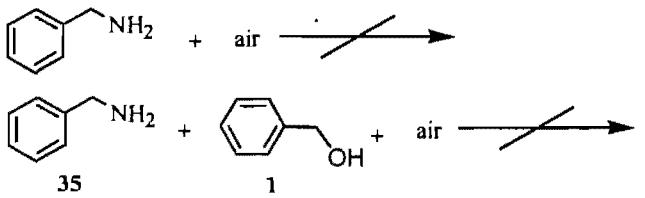


34 (Eq. 52)

3.1.1.12 Oxidation of benzyl amine

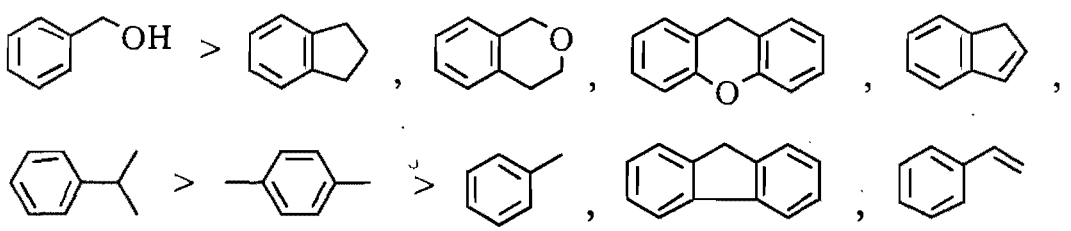
As shown in Run 14-1, benzyl amine could not be oxidized under air at 80 °C (Eq. 53). To find out if this lack of reactivity is due to deactivation of the catalyst in the presence of the amine, we tested the oxidation of benzyl alcohol in the presence of benzyl amine because benzyl alcohol is very easy to oxidize. Since benzyl

alcohol was not oxidized in the presence of benzyl amine, we conclude that this amine reacts with $Co(OAc)_2$ and hinders the oxidation (Run 14-2, Eq. 54).



3.1.1.13 Conclusions on oxidative reactions by $Co(OAc)_2$/NHPI in organic solvents

The above results indicate that the catalytic system composed of NHPI and $Co(OAc)_2$ is highly effective for the aerobic oxidation of a range of our target substrates. In organic solvents, this system can catalyze the oxidation of benzylic compounds in good conversion (> 40% for most substrates), but it is not suitable for oxidizing substrates not possessing benzylic C-H bonds, e.g. cinnamic acid and chromone, or tertiary alcohols such as 2-phenyl-2-propanol; it is also not suitable for benzylamine. The latter substrate is believed to deactivate the Co species by complexation. The relative ease of oxidation efficiency for the substrates seems to follow the order shown below:



It should be emphasized that the quantitative aspect of the above data is somewhat tentative, especially for benzaldehyde. It is likely that alkyl hydroperoxides gener-

ated during the oxidation reaction undergo decomposition when heated in the injection inlet of the GC; this would undermine the accuracy of the data. Additionally, although Iwahama and co-workers mentioned that MCBA could exert efficient rate enhancement of aerobic oxidation,[37] we found that MCBA did not enhance the oxidative rate of toluene, benzyl alcohol, and styrene oxidations in air. Therefore, MCBA was not used in most of aerobic oxidations of substrates.

3.1.2 Oxidation reactions in aqueous media

The purpose of our project is to eliminate or decrease organics present in bauxite (0.1-0.2%). We hope to pre-treat bauxite ore by using combinations of NHPI and transition metal salts. It is clear that pre-treatment of bauxite cannot be carried out in organic solvents from the economic and environmental viewpoints. Moreover, the treated ore is to be used in the Bayer process, which happens in base solutions. Hence, it is required that pre-treatment of bauxite be done in aqueous media. We have studied the catalytic activities of the system of $Co(OAc)_2$ and NHPI in the presence of water. During this phase of our studies, the most important problem to overcome was the diminished oxidation reactivity in reactions containing water. It is worth pointing out that the limited solubility of the substrates is the main obstacle for carrying out oxidation reactions in aqueous media. Our attention has, therefore, been focused on improving the efficacy of our oxidation protocol in aqueous media. The influence of the quaternary ammonium salt Bu_4NBr, sodium dodecyl sulphate, and benzalkonium chloride were studied to evaluate the effectiveness of these phase transfer agents in facilitating the oxidation reaction. A

number of experiments were carried out in mixtures of water or dilute alkaline solutions and organic solvents miscible with water in order to determine the suitability of aqueous media for the catalytic system consisting of $Co(OAc)_2$ / NHPI / O_2. In addition, it is known that dilute alkaline solutions can be used to increase the solubility of substrates possessing acidic hydrogen. Therefore, the influence of dilute alkaline solutions was also tested. In these oxidations, we selected indane, isochroman, *p*-xylene, benzyl alcohol, and xanthene as substrates for these oxidative reactions because of their high oxidation reactivity in organic solvents. Fluorene was also chosen because fragments with similar structures are found in bauxite. The results of these studies are presented below. These studies employed the procedure B for oxidation reactions under 1 atm of dioxygen.

3.1.2.1 Oxidation of benzyl alcohol

Benzyl alcohol is very easy to oxidize in ethyl acetate, even at room temperature. However, as can be seen from the following results (Table 18), water is not an optimum solvent for this system; indeed, even small amounts of it in a miscible co-solvent hinder the oxidation reaction greatly, even at high temperature. On the other hand, dilute alkaline solution is completely unsuitable for this system (Table 18, Runs 10 and 11). The oxidative efficiency was greatest in the mixture of THF and water (Table 18, Run 6).

Table 18: Oxidations of benzyl alcohol by $Co(OAc)_2$ / NHPI in aqueous media

Run	Solvent (8mL)	Appearance	$Co(OAc)_2$ (mol%)	NHPI (mol%)	Bu_4NBr (mol%)	Conv. (mol%)	Product Yield (mol%)	
							Benz-aldehye	Benzoic acid
1	H_2O (8)	Colorless, cloudy	0.5	10	--	0	--	--
2	H_2O (8)	Colorless, cloudy	0.5	10	6	0	--	--
3	H_2O (8)	Colorless, cloudy	2	15	10	0	--	--
4	H_2O (3) / Acetone (5)	Pale yellow, cloudy	0.5	10	--	0	--	--
5	H_2O (1) / Acetone (7)	Pale yelllow, clear	2	20	--	24	24	--
6*	H_2O (1) / THF (7)	Pale pink, clear	2	20	--	86	16	70
7	H_2O (1) / CH_3OH (7)	Yellow, cloudy	2	20	--	0	--	--
8	H_2O (1) / CH_3CN (7)	Pale yellow, clear	2	20	--	40	40	--
9	H_2O (3) / CH_3CN (5)	Pale yellow, clear	1	15	--	8	8	--
10	0,1N NaOH solution (8)	Cloudy pink precipates	2	15	Benzalk-onium chloride (1%)	0	--	--
11	0,1N NaOH (3) / CH_3CN (5)	Violet pre-cipates, cloudy	2	15	Benzalk-onium chloride (1%)	0	--	--

* Part of THF solvent was also oxidized into gamma-hydroxybutyric acid ($C_4H_8O_3$).

3.1.2.2 Oxidation of indene

Table 19 lists the comparison of indene oxidations in various aqueous media. Indene was oxidized fairly easily in a mixture of water and acetronitrile (Run 4), but the oxidation reactivity decreased in water alone (Run 1) or in the presence of other water-miscible organic solvents, especially THF (Run 2-3). On the other hand, although the oxidation can proceed well in water without surfactants, surfactants can improve the oxidative efficiency further (Run 1 and Run 6-7). Addition-

ally, the oxidative efficiency in the 0.1 N NaOH solution is better than the one in water (Run 7-8); but dilute alkaline solution had a negative influence on oxidation in the mixtures of aqueous solutions and acetronitrile (Run 4-5). In addition, it is worth noting that during the work-up of the reaction mixture we found only unreacted indene and trace of oxidized products in organic extraction layers. The fate of the oxidized products is not known yet, but we suspected that they remained in the aqueous layer or reacted with metal ions to generate precipitates, and we did not identify or isolate the oxidized products from aqueous layer or precipitates because our attention is focused on the degradation of substrates rather than analyzing the oxidized products.

Table 19: Indene oxidations catalyzed by $Co(OAc)_2$ / NHPI in aqueous media

Run	Solvent (Total 8mL)	Temp. (°C)	Surfactant	Appearance	Conv. (mol%)
1	H_2O (8)	60	--	Yellow, cloudy	62
2	H_2O (3) / Acetone (5)	80	--	Yellow, cloudy	51
3	H_2O (3) / THF (5)	60	--	Orange, cloudy	0
4	H_2O (3) / CH_3CN (5)	60	--	Yellow, cloudy	71
5	0.1N NaOH (3) / CH_3CN (5)	60	--	Orange, cloudy	22
6	H_2O (8)	60	Bu_4NBr (10 mol%)	Orange, cloudy	92
7	H_2O (8)	60	Benzalkonium chloride (1 mol%)	Yellow, cloudy	71
8	0.1N NaOH	60	Benzalkonium chloride (1 mol%)	Dark brown , cloudy,	80

3.1.2.3 Oxidation of isochroman

Isochroman was oxidized into 1-isochromanone (**32**) in mixtures of water and water-miscible solvents except THF (Run 2-4 in Table 20). But no oxidation took place in water without the help of surfactant (Run 1 in Table 20).

Table 20: Isochroman oxidations by $Co(OAc)_2$ / NHPI in aqueous media

Run	Solvent (Total 8 mL)	Appearance	Conv. (mol%)
1	H_2O without surfactant	Yellow cloudy	0
2	Acetone (5 mL)/H_2O (3 mL)	Light Yellow, clear	60
3	CH_3CN (5 mL)/H_2O (3 mL)	Light Yellow, clear	24
4	THF (5 mL)/H_2O (3 mL)	Light Yellow, cloudy	0

The influence of adding surfactants on the oxidation reaction in water has been studied, as shown below (Table 21). A number of bi-phasic surfactants can enhance the oxidation reactivity, and benzalkonium chloride has the best influence of these surfactants tested.

Table 21: Isochroman oxidations catalyzed by $Co(OAc)_2$ / NHPI in water with or without surfactants

Run	Surfactant	Appearance	Conv. (mol%)
1	--	Yellow cloudy	0
2	Bu_4NBr (6 mol%, 58,6 mg)	Light Yellow, cloudy	63
3	Sodium dodecyl sulfate (6 mol%, 52,7 mg)	Light Yellow, cloudy	50
4	Benzalkonium chloride* (63 mg, 6 mol%)	White, cloudy	74

* $PhCH_2N(Me)_2RCl$ (R = C_8H_7 to $C_{18}H_{37}$, predominantly $C_{12}H_{25}$)

We have also examined the influence of different concentrations of benzalkonium chloride on the oxidation reaction, as shown below (Table 22). Based on these results, 1 mol% benzalkonium chloride has been used in most other oxidations of substrates.

Table 22: Isochroman oxidations catalyzed by $Co(OAc)_2$ / NHPI with various concentration of surfactant

Run	Benzalkonium chloride	Appearance	Conv. (mol%)
1	13.2 mg, 1.26%	Slight Yellow, cloudy	64
2	21.1 mg, 2.01%	Slight Yellow, cloudy	50
3	37.5 mg, 3.57%	Slight Yellow, cloudy	64
4	47.3 mg, 4.50%	Slight Yellow, cloudy	50

Next, we studied the influence of alkaline solution on the oxidative efficiency (Table 23). With the help of 1 mol% benzalkonium chloride, isochroman was oxidized in dilute alkaline solutions and water. The 0.1 N NaOH solution or the 0.1 N $NaHCO_3$ solution could strengthen the oxidative efficiency (Runs 2 and 5), whereas solutions of low-concentrated NaOH gave poor results (Runs 3 and 4). Oxidation of isochroman also proceeded better in the mixtures of alkaline solutions and acetonitrile without the help of surfactant, compared to the one in the mixture of water and acetonitrile (Run 6-8).

Table 23: Comparison of isochroman oxidation catalyzed by $Co(OAc)_2$/NHPI in various basic aqueous media

Run	Solvent (8 mL)	pH of aqueous solutions	Appearance	Conv. (mol%)
1	H_2O with 1 mol% benzalkonium chloride	5	Yellow cloudy	29
2	0.1N $NaHCO_3$ solution with 1 mol% benzalkonium chloride	10.5	Dark brown cloudy	54
3	0.001N NaOH solution with 1 mol% benzalkonium chloride	9	Yellow cloudy	18
4	0.01N NaOH solution with 1 mol% benzalkonium chloride	10	Yellow cloudy	13
5	0.1N NaOH solution with 1 mol% benzalkonium chloride	13	Black cloudy	46
6	CH_3CN (5) / H_2O (3)	5	Light yellow clear	29
7	CH_3CN (5) / 0.1 N NaOH (3)	13	Yellow clear	94
8	CH_3CN (5) / 0.1 N $NaHCO_3$ (3)	10.5	Orange clear	95

3.1.2.4 Oxidation of fluorene

Table 24 lists all tests results of fluorene oxidation in aqueous media, which proved that oxidation of fluorene could not happen in all conditions tested, even at high temperature or using more surfactant.

Table 24: Oxidations of fluorene by $Co(OAc)_2$ / NHPI in aqueous media

Run	Solvent	Bu_4NBr (mol%)	Appearance	Temp. (°C)	Conv. (mol%)
1	H_2O (9 mL)	10%	Yellow, cloudy	88-102	0%
2	H_2O (3 mL) / CH_3CN (5 mL)	--	cloudy, pink precipitates	70	0%
3	H_2O (3 mL) / THF (5 mL)	--	cloudy, pink precipitates	70	0%
4	H_2O (3 mL) / Acetone (5 mL)	--	Yellow, cloudy	70	0%
5	H_2O (6 mL) / Acetone (10 mL)	--	Light yellow cloudy, white precipates	80	0%
6	0,1N NaOH (6 mL) / Acetone (10 mL)	--	Slight pink cloudy, pink precipates	80	0%
7	0,1N $NaHCO_3$ (6 mL) / Acetone (10 mL)	--	Light yellow cloudy, white precipates	80	0%

3.1.2.5 Oxidation of indane

Table 25 lists the results of oxidation of indane in aqueous media. As can be seen, benzalkonium chloride can greatly enhance the catalytic oxidative efficiency in water (Run 1-2). However dilute alkaline solutions can decrease the oxidative efficiency of indane (Runs 2-5), especially the low-concentrated NaOH solution. Meanwhile, oxidation of indane was hindered in the mixture of water-miscible organic solvents and water (Runs 6-8). It is worth noting that the oxidized products of oxidations of indane could not be found in organic extraction layers, and this situation was similar to the one that happened in aqueous oxidations of indene.

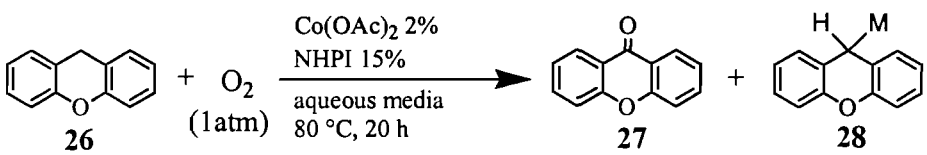
Table 25: Indane oxidations catalyzed by $Co(OAc)_2$ / NHPI in aqueous media

Run	Solvent (total 8mL)	Benzalkonium chloride (mol%)	Appearance	Conv. (mol%)
1	H_2O	---	Yellow cloudy	7%
2	H_2O	1 mol%	Yellow cloudy	83%
3	0.1N $NaHCO_3$ solution	1 mol%	Dark gray, cloudy	34%
4	0.001N NaOH solution	1 mol%	Dark gray, cloudy	7%
5	0.1N NaOH solution	1 mol%	Dark gray, cloudy	67%
6	H_2O (3) / Acetone (5)	---	Light Yellow, cloudy	0
7	H_2O (3) / CH_3CN (5)	---	Light Yellow, cloudy	0
8	H_2O (3) / THF (5)	---	Light Yellow, cloudy	0

3.1.2.6 Oxidation of xanthene

Xanthene was oxidized with good conversions in aqueous conditions (Table 26). The main product is xanthone **(27)**, plus the unknown compound **28** (minor product) and traces of xanthenol. The bi-phasic surfactant benzalkonium chloride enhances the oxidative efficiency (Run 1-2), whereas alkaline media reduces the oxidation efficiency (Runs 2-5).

Table 26: Xanthene oxidations by $Co(OAc)_2$ / NHPI in aqueous media*[a]



Run	Solvent (total 8mL)	pH of solution	Benzalkonium chloride	Conv. (mol%)	Products (yield mol%)	
					27	28*[b]
1	H_2O	5	--	21%	8%	≅3%
2	H_2O	6	1 mol%	36%	10%	≤1%
3	0.001N NaOH solution	9	1 mol%	16%	5%	≅1%
4	0.1N NaOH solution	13	1 mol%	14%	3%	≅1%
5	0.1N $NaHCO_3$ solution	10.5	1 mol%	10%	3%	≤1%

*[a] Based on NMR tests. *[b] The % yield of compound **28** was estimated from peak area in GC/MS spectra.

3.1.2.7 Oxidation of *p*-xylene

As shown in Table 27, the oxidation of *p*-xylene in the mixture of acetonitrile and water was more facile than those in aqueous mixtures of acetone or THF (Runs 1-3). For oxidation of *p*-xylene, this catalyst system gave high conversion without the help of surfactant (Run 4). Surfactants or phase-transfer reagents can further enhance on oxidative efficiency (Runs 5 and 6). In addition, NaOH solutions decreased the oxidative reactivity (Run 7-8). As before, the oxidized products of *p*-xylene could not be found in organic extracting layer.

Table 27: *p*-Xylene oxidations in aqueous media by $Co(OAc)_2$ / NHPI

Run	Solvent (8mL)	Surfactant (mol%)	Appearance	Conv. (mol%)	4-methyl-benzaldehyde (Yield, mol%)*
1	Acetone (5) / H_2O (3)	--	Yellow, cloudy	22	1
2	CH_3CN (5) / H_2O (3)	--	Yellow, clear	66	0,4
3	THF (5) / H_2O (3)	--	Light orange, cloudy	20	0,7
4	H_2O	--	Light yellow, cloudy	62	--
5	H_2O	Bu_4NBr (10 mol%)	Light yellow, cloudy	92	trace
6	H_2O	Sodium dodecylsulfate (10 mol%)	Yellow, clear with foams	71	--
7	H_2O	Benzalkonium chloride (1 mol%)	Light yellow, cloudy	89	--
8	0.01N NaOH	Benzalkonium chloride (1 mol%)	Light yellow, cloudy	59	--

* The compound refers to products found in organic extracts.

3.1.2.8 Conclusion on oxidations of substrates in aqueous media

In sum, oxidation reactivity of the substrates is diminished greatly in aqueous media compared to aerobic oxidations in organic solvents. Fluorene cannot be

oxidized, and oxidation of benzyl alcohol is deactivated, even in the presence of a very small amount of water. Fortunately, phase transfer surfactants, eg., benzalkonium chloride, can usually enhance the oxidative efficiency. Among the organic solvents examined, acetone or acetonitrile can improve the oxidation reactivity of substrates except indane. Interestingly, pure THF can be miscible with water, but when substrates are added in the mixture of THF and water, the THF layer separates from water, while cobalt acetate remains in the water layer, so that no oxidation happens for most of substrates. In contrast, the oxidation of benzyl alcohol proceeds fairly well in the mixture of THF and water, although part of THF is oxidized. Additionally, higher levels of pH have different (even contradictory) influences on aerobic oxidations of substrates in aqueous media, depending on the conditions. For example, in oxidation of indene, the oxidative efficiency was enhanced in the 0.1 N NaOH solution compared to the reaction in water (Run 7-8 in Table 31), but when a 0.1 N NaOH solution was combined with acetonitrile, the oxidative efficiency was decreased greatly (Run 3-4 in Table 18).

3.2 Aerobic oxidations catalyzed by iron catalysts/NHPI

3.2.1 Aerobic oxidations in ethyl acetate

Since bauxite contains a significant amount of iron oxides that are potentially effective for aerobic oxidations, we examined the oxidative efficiency of the combinations of iron salts and NHPI. Isochroman was chosen to evaluate the catalytic efficiency of iron salts. Additionally the commercial prices of these ironic cata-

lysts are compared when considering their influences on oxidation. We examined the oxidation of isochroman (3 mmol) by 5 mol% of iron salts and 10 mol% NHPI in ethyl acetate at 60 °C under 1 atm of dioxygen for 20 h (experimental details are described in Procedure C on page 54), and the results are described in Table 28. According to these results, four iron salts, $Fe(NO_3)_3 \cdot 9H_2O$, $FeSO_4 \cdot 7H_2O$, Fe_2O_3 and $Fe(OAc)_2$ give good results; all of these iron salts are inexpensive except $Fe(OAc)_2$. Fe_2O_3 is the most attractive since it exists in bauxite, and we used $Fe(NO_3)_3 \cdot 9H_2O$, $FeSO_4 \cdot 7H_2O$, and Fe_2O_3 to determine the catalytic oxidative effects of more substrates in ethyl acetate. Table 29 lists the results of oxidations, which shows that the best overall catalyst is $Fe(NO_3)_3 \cdot 9H_2O$ followed closely by Fe_2O_3. The products of substrate oxidations catalyzed by Fe/NHPI are similar to those catalyzed by Co(II)/NHPI, except in the case of indane, where 1,3-indanedione was found, which didn't exist in oxidized products of indane catalyzed by cobalt acetate/NHPI.

Table 28: Selection of proper iron catalysts from oxidations of isochroman

Run	Ironic catalysts	Grade	Price* (CAD$ per mol)	Conv. (mol%)
	$Co(OAc)_2 \cdot 4H_2O$	Reagent grade	$33.13	100%
1	$FeSO_4 \cdot 7H_2O$	ReagentPlus®, ≥99.0%	$12.33	93%
2	$FeCl_2 \cdot 4H_2O$	ReagentPlus®, 99.0%	$32.73	0%
3	$FeCl_3 \cdot 6H_2O$	Reagent grade, ≥98.0%, purified lumps	$29.93	0%
4	$Fe(acac)_3$	97%	$147.46	51%
5	$Fe(NO_3)_3 \cdot 9H_2O$	ACS reagent, ≥98.0%	$46.01	100%
6	$Fe(OAc)_2$	95%	$1171.74	100%
7	Fe_2O_3	Powder, <5 μm, ≥99.0%	$7.16	93%

*The prices come from Sigma-Aldrich Catalogue (2007-2008).

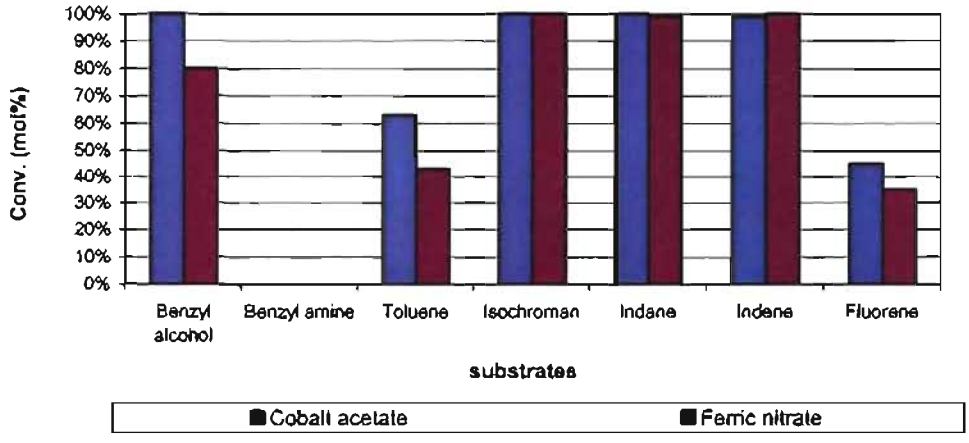
Table 29: Comparison of oxidative efficiencies catalyzed by various iron salts combined with NHPI

	Iron Salts		Fe_2O_3	$Fe(NO_3)_3 \cdot 9H_2O$	$FeSO_4 \cdot 7H_2O$
Substrates	**Isochroman (Conv. mol%)**		**93%**	**100%**	**93%**
	Benzylamine (Conv. mol%)		**0%**	**0%**	**0%**
	Benzyalcohol (Conv. mol%)		**88%**	**80%**	**3%**
	Product yield (mol%)	Benzaldehyde	17%	32%	3%
		Benzoic acid	71%	48%	0%
	Toluene (Conv. mol%)		**11%**	**43%**	**0%**
	Product yield (mol%)	Benzyl alcohol	1%	--	--
		Benzaldehyde	7%	3%	trace
		Benzoic acid	trace	40%	--
	Indene (Conv. mol%)		**69%**	**100%**	**43%**
	Product yield (mol%)[*1]	2-Methyl-benzaldehyde	14%	2%	10%
		2-Indanone	4%	4%	2%
		Benzenedicarboxaldehyde	--	3%	--
		Phthalide	--	3%	--
		2-Formyl benzoic acid	--	4%	--
	Fluorene (Conv. Mol%) [*2,3]		**6%**	**35%**	**17%**
	Product yield (mol%)	9-Flurenone[*4]	--	--	--
	Indan (Conv. Mol%)		**58%**	**99%**	**58%**
	Product yield (mol%)	1-Indanol	12%	11%	9%
		1-Indanone	21%	39%	19%
		1,3-Indandione[*1]	--	8%	--
		Phthalide[*1]	--	1%	--

[*1] Yields were based on NMR tests.
[*2] The oxidation of fluorene was carried out at 70°C, all other oxidations at 60°C.
[*3] Fluorene oxidations were analyzed by NMR tests.
[*4] In NMR spectra of fluorene oxidations, the peaks of 9-fluorenone were obscured by those of other compounds so that 9-fluorene could not be quantified by using NMR, but was identified by GC/MS tests.

Overall, $Fe(NO_3)_3 \cdot 9H_2O$ is the best of all tested iron catalysts. Figure 12 shows the comparison of aerobic oxidations catalyzed by NHPI combined with cobalt acetate and ferric nitrate. These results show that the catalytic efficiency of ferric nitrate almost reached that of $Co(OAc)_2$ when a large proportion of iron-based catalysts was used (5 mol% Fe compared to 0.5 mol% Co).

Figure 12: Comparison of aerobic oxidations catalyzed by NHPI combined with cobalt acetate (0.5%) or ferric nitrate (5%)



In the next phase of our studies, $Fe(NO_3)_3 \cdot 9H_2O$ and Fe_2O_3 were employed to evaluate their catalytic reactivities in aerobic oxidations in a variety of aqueous media.

3.2.2 Aerobic oxidations in aqueous media

Isochroman, indane, and xanthene (solid) were used as substrates to evaluate the oxidative efficiency of the system of Fe_2O_3 or $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI in aqueous oxidations. These experiments were conducted using 10 mol% of iron salts and 15 mol% of NHPI under 1 atm of dioxygen (experimental details are described in Procedure D on page 54). Benzalkonium chloride was used as surfactant to evaluate its influence on the oxidative efficiency. Various dilute alkaline solutions were also evaluated to determine their influence on catalytic efficiency. In oxidative reactions, these three substrates were oxidized partially,

isochroman giving isochromanone (**32**) and xanthene giving xanthone (**27**). As observed in the case of oxidations catalyzed by $Co(OAc)_2$, indane was consumed in aqueous oxidations, but the oxidized products of indane could not be found in organic solvent extraction phases, and only a trace of 1-indanol or 1-indanone was found. Tables 30-32 list the test results, which are compared to the results of the $Co(OAc)_2$/NHPI system.

Table 30: Comparison of catalytic oxidations of indane by NHPI in various aqueous solutions combined with iron salts or cobalt acetate

Run	Solvent (total 8 mL)	Benzalkonium chloride (mol%)	pH of solvent	Conversion (mol%)		
				$Co(OAc)_2$	Iron catalysts	
					Fe_2O_3	$Fe(NO_3)_3 \cdot 9H_2O$
1	H_2O	---	5	7%	80%	45%
2	H_2O	1%	6	83%	81%	85%
3	0,001N NaOH solution	1%	9	7%	58%	84%
4	0,1N $NaHCO_3$ solution	1%	10.5	34%	83%	91%

The results listed in Table 30 show that benzalkonium chloride did not influence the oxidation of indane by the catalytic system of Fe_2O_3/NHPI, but it did improve the efficiency of aqueous oxidations promoted by $Fe(NO_3)_3 \cdot 9H_2O$/NHPI and especially that of the $Co(OAc)_2$/NHPI system. Generally, dilute alkaline solutions decreased the oxidative efficiency of oxidation of indane in the presence of Fe_2O_3 or $Co(OAc)_2$, especially the latter. As for the catalytic system of $Fe(NO_3)_3 \cdot 9H_2O$/NHPI, 0.001N NaOH solution did not have an obvious influence, whereas 0.1N $NaHCO_3$ solution increased the oxidative reactivity to some extent.

Table 31: Comparison of isochroman oxidations in various aqueous solutions catalyzed by NHPI combined with cobalt acetate or iron salts*

Run	Solvent (8 mL)	Benzalkonium chloride (mol%)	pH of solvent	$Co(OAc)_2$	Fe_2O_3		$Fe(NO_3)_3 \cdot 9H_2O$	
				Conv. (mol%)	Conv. (mol%)	32 yield (mol%)	Conv. (mol%)	32 yield (mol%)
1	H_2O	---	5	**0**	**51%**	16%	**34%**	20%
2	H_2O	1%	6	**29%**	**65%**	24%	**48%**	32%
3	0.001N NaOH solution	1%	9	**18%**	**52%**	24%	**59%**	17%
5	0.1N $NaHCO_3$ solution	1%	10.5	**54%**	**33%**	9%	**61%**	31%

* 1-Isochromanone **32** was quantified by NMR tests.

From the above results (Table 31), it is clear that benzalkonium chloride can improve the oxidative reactivity of isochroman for both iron catalyst systems and cobalt acetate system; dilute alkaline solutions have a negative influence for the catalytic system of Fe_2O_3/NHPI, while they have a positive influence when using the catalytic system of $Fe(NO_3)_3 \cdot 9H_2O$/NHPI. However, different alkaline solutions had different influences on oxidation of isochroman catalyzed by the system of $Co(OAc)_2$/NHPI: 0.001N NaOH solution decreased the oxidative efficiency, but 0.1N $NaHCO_3$ increased it.

Table 32: Comparison of xanthene oxidations in various aqueous solutions catalyzed by NHPI combined with cobalt acetate or iron salts *

Run	Solvent (8mL)	Benzalkonium chloride (mol%)	pH of solvent	$Co(OAc)_2$		Fe_2O_3		$Fe(NO_3)_3 \cdot 9H_2O$	
				Conv. (mol%)	27 yield (mol%)	Conv. (mol%)	27 yield (mol%)	Conv. (mol%)	27 yield (mol%)
1	H_2O	---	5	**21%**	8%	**2%**	1%	**6%**	2%
2	H_2O	1%	6	**36%**	10%	**3%**	2%	**26%**	13%
3	0.001N NaOH	1%	9	**16%**	5%	**4%**	4%	**10%**	4%
4	0.1N NaOH	1%	13	**14%**	3%	**2%**	1%	**8%**	0.3%
5	0.1N $NaHCO_3$	1%	10.5	**10%**	3%	**4%**	0.3%	**18%**	3%

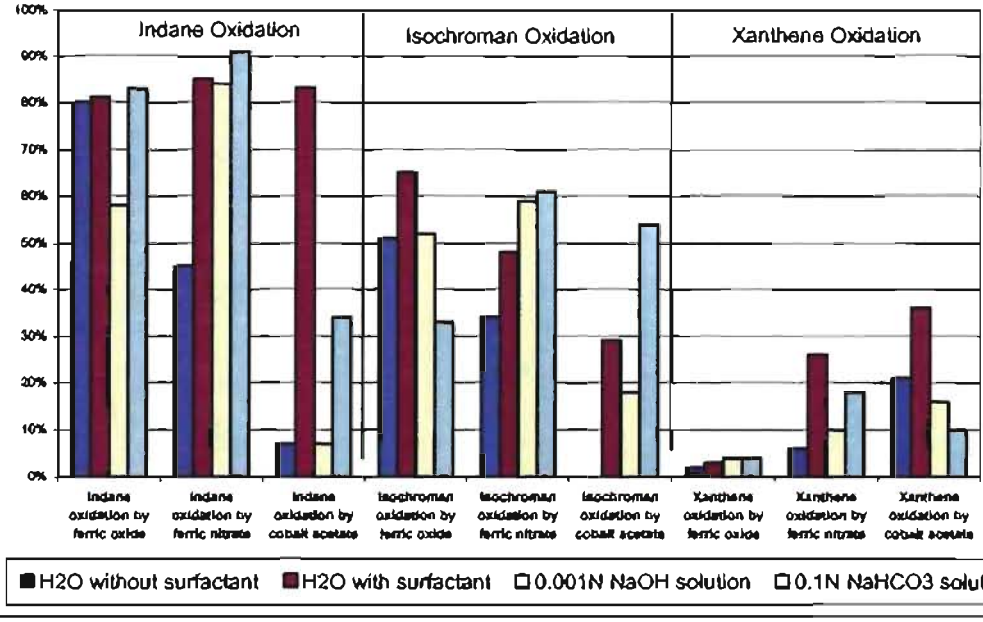
* These experiments were quantified by NMR tests.

The above results (Table 32) indicate that the catalytic system of Fe_2O_3/NHPI was not effective, and xanthene was hardly oxidized by this catalytic system. The catalytic system of $Fe(NO_3)_3{\cdot}9H_2O$/NHPI is better with 10-30 mol% of conversion, while the catalytic system $Co(OAc)_2$/NHPI has a little higher efficiency with 10-40 mol% of conversion. As for the catalytic system of $Fe(NO_3)_3{\cdot}9H_2O$/NHPI and the catalytic system $Co(OAc)_2$/NHPI, benzalkonium chloride improved the oxidative reactivity of xanthene, but dilute alkaline solutions have a negative influence.

Conclusions on catalytic oxidations using iron salts. In sum, Figure 13 compares aqueous oxidation of the above three substrates in various aqueous media in the presence of cobalt acetate or iron salts combined with NHPI. The two iron systems worked in aerobic oxidation of indane and isochroman as well as $Co(OAc)_2$. However, xanthene was more difficult to oxidize compared to the other two substrates, such that the catalytic system of Fe_2O_3/NHPI hardly worked. Moreover, the oxidative reactivity of xanthene in aqueous media seemed lower, and indane higher. Benzalkonium chloride could improve the oxidative efficiency, but dilute alkaline solutions had different influences depending on the reaction conditions. It was noted that oxidations using $Co(OAc)_2$ were more efficient in the presence of benzalkonium chloride, but little or no improvements were observed in iron-catalyzed oxidatons. In addition, the catalytic system of $Co(OAc)_2$/NHPI seems more sensitive to the change of aqueous media compared to the iron sys-

tems. Overall, it seems that $Fe(NO_3)_3 \cdot 9H_2O$/NHPI had the best catalytic efficacy for oxidations of all three substrates in aqueous media.

Figure 13 : Comparison of aqueous oxidations catalyzed by NHPI combined with cobalt acetate (2%) or iron catalysts (10 mol%)



3.3 Aerobic oxidations catalyzed by transition metal / 4-nitro-NHPI

4-Nitro-NHPI is easily soluble in water because of the introduction of the polar nitro group, therefore we decided to study its catalytic reactivity and compare it to that of NHPI, especially in aqueous media. First, 4-nitro-NHPI was evaluated in aerobic oxidation of substrates in ethyl acetate, compared to NHPI. Then the influence of the system of 4-nitro-NHPI and ferric nitrate in aqueous oxidations was also evaluated.

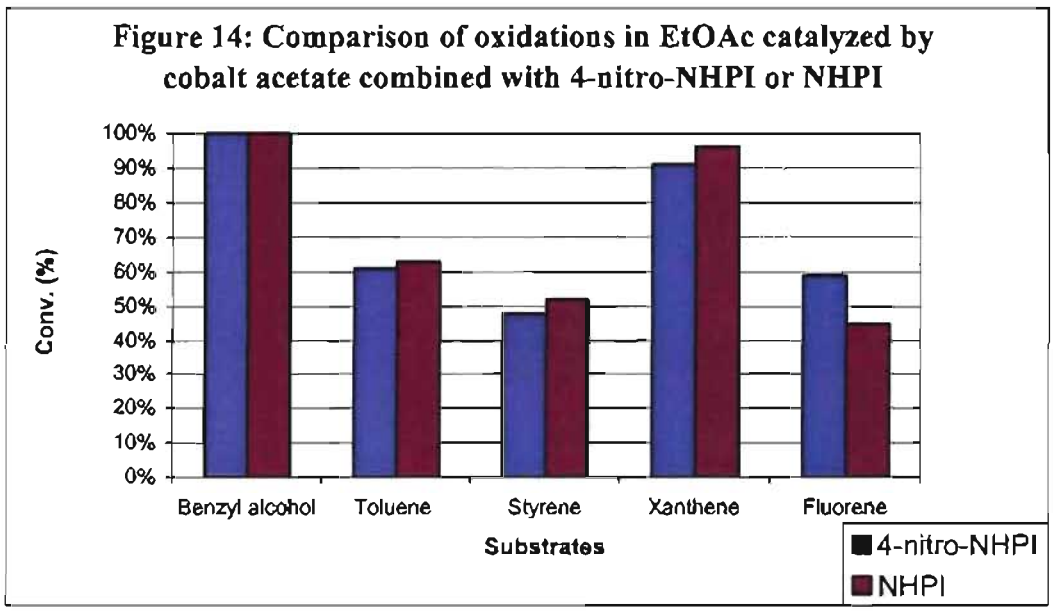
3.3.1 Aerobic oxidation by $Co(OAc)_2$ / 4-nitro-NHPI in EtOAc

The oxidation of benzyl alcohol, toluene, styrene, xanthene, and fluorene were studied using 3 mmol of the substrate, 0.5 mol% of $Co(OAc)_2$, and 10 mol% of 4-nitro-NHPI or NHPI under 1 atm of dioxygen in ethyl acetate to determine the relative reactivities of 4-nitro-NHPI. The experimental details are described in Procedure E on page 54, and the results are listed in Table 33 and shown in Figure 14. As can be seen, similar results were obtained with systems based on 4-nitro-NHPI or NHPI.

Table 33: Comparison of aerobic oxidations in EtOAc catalyzed by $Co(OAc)_2$ combined with 4-nitro-NHPI or NHPI

Substrates	Conv. (mol%)		Oxidized products	Yield (mol%)	
	4-nitro-NHPI	NHPI		4-nitro-NHPI	NHPI
Benzyl alchohol	100%	100%	Benzoic acid	99%	99%
			Benzaldehyde	Trace	Trace
Toluene	61%	63%	Benzaldehyde	1%	1%
			Benzoic acid	55%	54%
Styrene	48%	52%	Benzaldehyde	13%	12%
			Unknown compound (RT=15.7)	--	≅7%*1
			Diphenylethanedione	≅5%*1	5%*2
			Styrene oxide	≅2%*1	2% *2
			1-Phenyl-1,2-ethane-diol	≅1%*1	≅1%*1
			Benzoic acid	2%	2%
Xanthene	91%	96%	Xanthone	33%	62%
			Compound **28** (RT=17.72)	≅10%*1	≅14%*1
			9-Xanthenol	≅3%*1	≅1%*1
			2-Hydroxy-benzophenone	Trace	Trace
Fluorene*3	59%	45%	9-Fluorenone	44%	44%

*1 The yields were estimated from the peak areas in GC/MS spectra. Accurate quantification was not possible because samples of authentic products were not available. *2 Based on NMR tests. *3 Aerobic oxidation of fluorene was carried out at 70°C, others at 60°C.



3.3.2 Aerobic oxidation catalyzed by $Fe(NO_3)_3 \cdot 9H_2O$/4-nitro-NHPI in aqueous media

The aqueous oxidation of benzyl alcohol, indane, isochroman, and xanthene (3 mmol) catalyzed by $Fe(NO_3)_3 \cdot 9H_2O$ (10 mol%) combined with NHPI or 4-nitro-NHPI (15 mol%) were studied in order to compare the reactivities of these co-catalysts. Experimental details are described in procedure F on page 54, and the results are discussed below.

3.3.2.1 *Oxidation of benzyl alcohol*

The oxidation of benzyl alcohol was less efficient in water, giving only 7 mol% conversion and 1% of benzaldehyde even when the reaction was carried out in the presence of benzalkonium chloride (1 atm of dioxygen, 80°C).

3.3.2.2 Oxidation of indane

Indane was oxidized in aqueous media with a good conversion (50-60%, see Table 34). As was the case in the aqueous oxidation of indane catalyzed by $Co(OAc)_2$/NHPI, we were not able to isolate the products of indane oxidation reactions, but the conversion rates could be determined. Comparison of the results shows that NHPI was in most cases somewhat more efficient than 4-nitro-NHPI. The oxidation reactions promoted by both 4-nitro-NHPI and NHPI were more efficient in the presence of benzalkonium chloride, whereas strongly alkaline media had a negative influence on the catalytic activities. Interestingly, using $NaHCO_3$ as base increased the oxidative efficiency to some extent.

Table 34: Aerobic oxidations of indane catalyzed by $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI or 4-nitro-NHPI in aqueous media

Run	Solvent	pH of solvent	Benzalkonium chloride	Conv. (mol%)	
				NHPI	4-nitro-NHPI
1	H_2O	5	--	45%	49%
2	H_2O	6	1 mol%	85%	62%
3	0.001N NaOH	9	1 mol%	84%	61%
4	0.1N NaOH	13	1 mol%	25%	58%
5	0.1N $NaHCO_3$	10.5	1 mol%	91%	54%

3.3.2.3 Oxidation of isochroman

Isochroman was oxidized into 1-isochroman (**32**) in aqueous media with good conversion (37-77%, Table 35). As for the oxidation of indane, oxidation efficiency increased in the presence of benzalkonium chloride but suffered in strongly alkaline aqueous media.

Table 35: Aerobic oxidations of isochroman by $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI or 4-nitro-NHPI in aqueous media

Run	Solvent	pH of solvent	Benzalkonium chloride	NHPI		4-nitro-NHPI	
				Conv. (mol%)	32 (Yield, mol%)	Conv. (mol%)	32 (Yield, mol%)
1	H_2O	5	--	34%	20%	49%	15%
2	H_2O	6	1 mol%	48%	32%	61%	29%
3	0.001N NaOH	9	1 mol%	59%	17%	77%	28%
4	0.1N NaOH	13	1 mol%	42%	28%	39%	11%
5	0.1N $NaHCO_3$	10.5	1 mol%	61%	31%	37%	12%

3.3.2.4 Oxidation of xanthene

Xanthene was oxidized to xanthone (**27**) with low conversions in aqueous media (11-22%, Table 36). The influence of benzalkonium chloride and strongly alkaline conditions were similar to the oxidations of indane and isochroman.

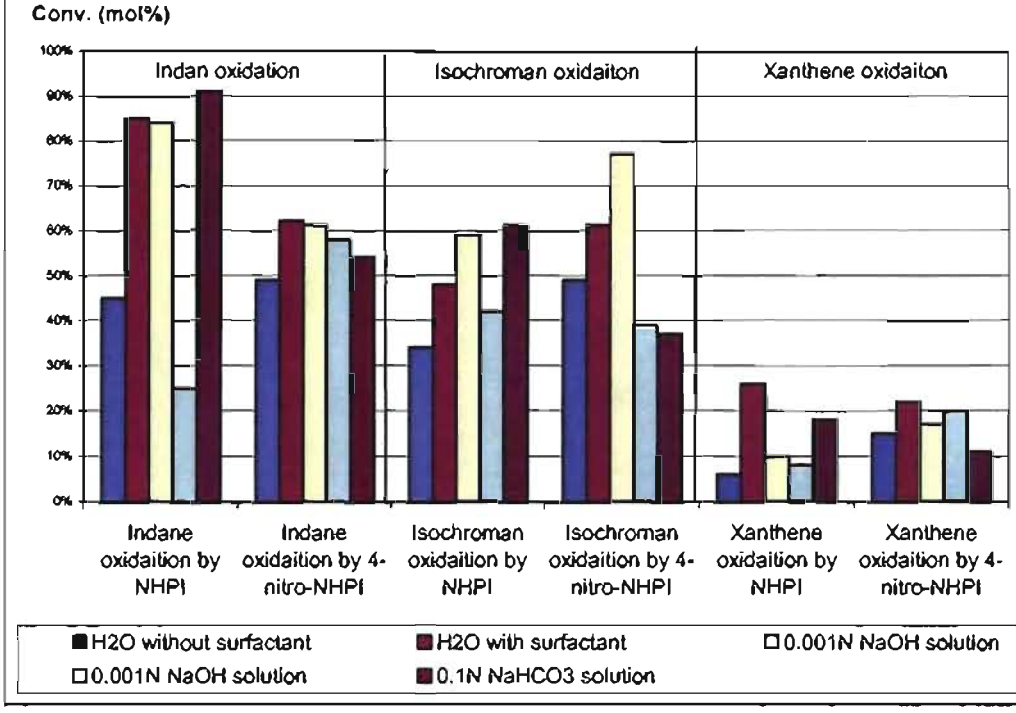
Table 36: Aerobic oxidations of xanthene by $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI or 4-nitro-NHPI in aqueous media

Run	Solvent	pH of solvent	Benzalkonium chloride	NHPI		4-nitro-NHPI	
				Conv. (mol%)	27 (Yield, mol%)	Conv. (mol%)	27 (Yield, mol%)
1	H_2O	5	--	6%	2%	15%	5%
2	H_2O	6	1 mol%	26%	13%	22%	9%
3	0.001N NaOH	9	1 mol%	10%	4%	17%	5%
4	0.1N NaOH	13	1 mol%	8%	0.3%	20%	1%
5	0.1N $NaHCO_3$	10.5	1 mol%	18%	3%	11%	2%

3.3.2.5 Comparison of aqueous oxidations by $Fe(NO_3)_3 \cdot 9H_2O$ combined with NHPI or 4-nitro-NHPI

Figure 15 shows that aqueous oxidations are somewhat less efficient by 4-nitro-NHPI compared to NHPI, but oxidations using the latter seem to be more sensitive to reaction conditions.

Figure 15: Comparison of aqueous oxidations catalyzed by ferric nitrate combined with NHPI or 4-nitro-NHPI



Chapter 4: Aerobic Oxidations of Humic Acids and Bauxite

The results described in the previous chapter show that the catalytic system consisting of cobalt or iron salts and NHPI is quite effective for oxidations of various hydrocarbons, even in aqueous media. Since organics in bauxite exist in the form of humic substances, we have studied the effectiveness of this catalytic system for oxidation of humic acids in water or dilute alkaline solutions. We have also evaluated the oxidative efficacy of the catalytic system in aerobic oxidation of bauxite. In addition, since the previous results showed that Fe_2O_3, which is relatively abundant in bauxite, is also a competent catalyst for oxidations, we have tested the oxidations of bauxite catalyzed by NHPI only, without the addition of metal salts. As will be explained, UV-vis spectroscopy was used to monitor aerobic oxidations of bauxite. In addition, we have probed the individual properties of $Co(OAc)_2$, NHPI and their mixture before studying oxidations of bauxite and humic acid sodium salt.

4.1 NHPI and $Co(OAc)_2$: UV-vis spectroscopy and thermal stability in aqueous media

Figure 16 shows the UV-vis spectrum of NHPI, which is dissolved in water and has two main absorption bands at 222 nm (strong) and 300 nm (medium).

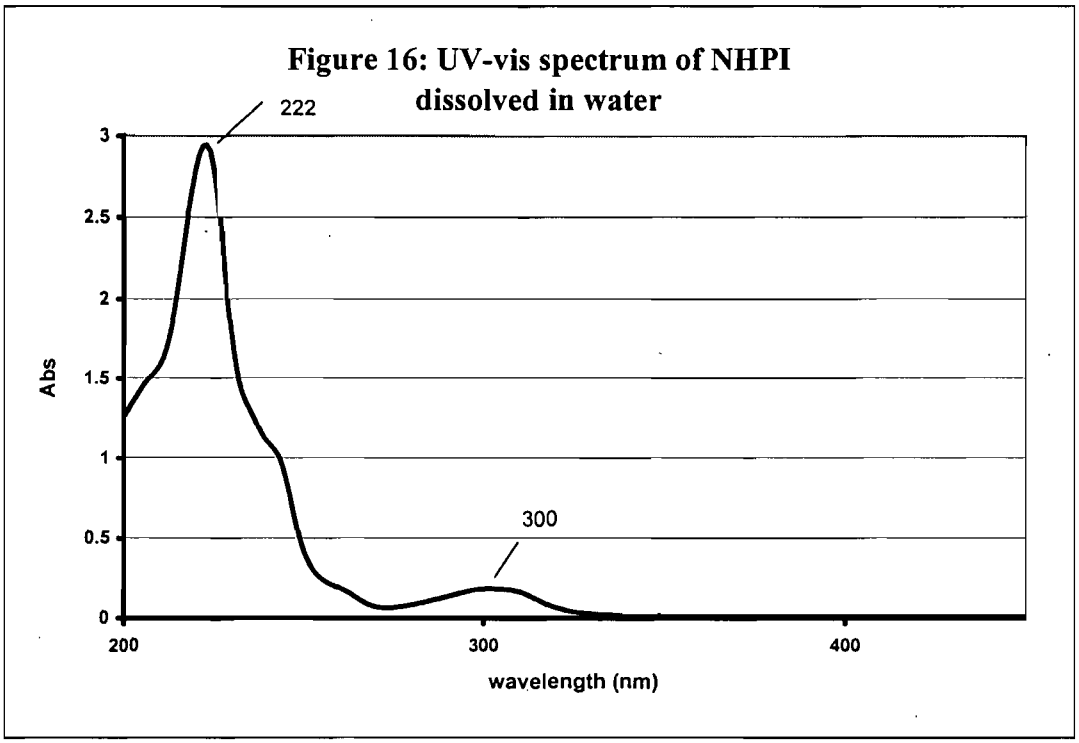
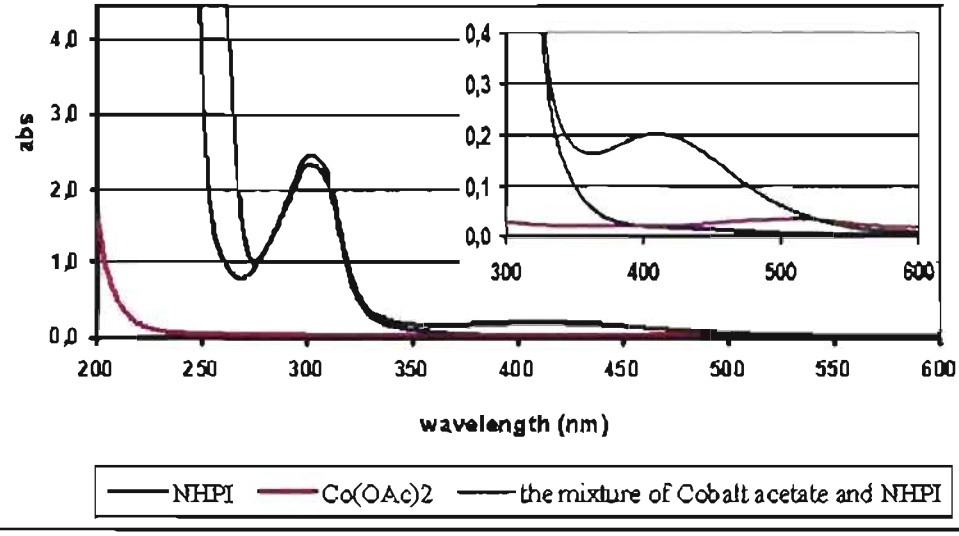


Figure 17 compares the UV-vis spectra of NHPI, $Co(OAc)_2$, and a mixture of both. Cobalt acetate has a weak absorption band at 512 nm, which corresponds to a cobalt-centred transition. When cobalt acetate was added into the solution of NHPI, the solution turned from pale yellow to dark yellow as a new complex was generated; the absorption band at 512 nm of cobalt acetate disappeared, and a new absorption band at 407 nm appeared which comes from the new complex. We believe that the new complex of NHPI and $Co(OAc)_2$ is an important intermediate for the generation of PINO radicals.

Figure 17: UV-vis spectrum of NHPI, cobalt acetate, and the mixture of NHPI and cobalt acetate



In addition, NHPI is not so stable in water, especially at high temperature. When the aqueous NHPI solution was kept for around 1 month, NHPI decomposed (see the pink line in Figure 18). Dioxygen had no influence on this decomposition (compare the green and violet traces in Figure 18), but higher temperatures accelerated it (see the light orange trace in Figure 18) such that complete decomposition took place even after 2 hours at 80 °C (Figure 19). After NHPI decomposition, the absorption band at 300 nm of NHPI disappeared, and a new absorption band at 280 nm appeared. When GC/MS was used to analyze the samples after oxidation of substrates catalyzed by $Co(OAc)_2$/NHPI/O_2 (1 atm) in ethyl acetate or aqueous media, phthalic anhydride (RT= 5.31) and phthalimide (RT= 7.31) were always found, which are the possible decompostion products of NHPI. The UV-vis spectrum shown in Figure 20 indicates that heating NHPI for 22 h at 80 °C in water converts it to phthalic anhydride.

Figure 18: UV-vis spectrum of aqueous NHPI solutions at various conditions

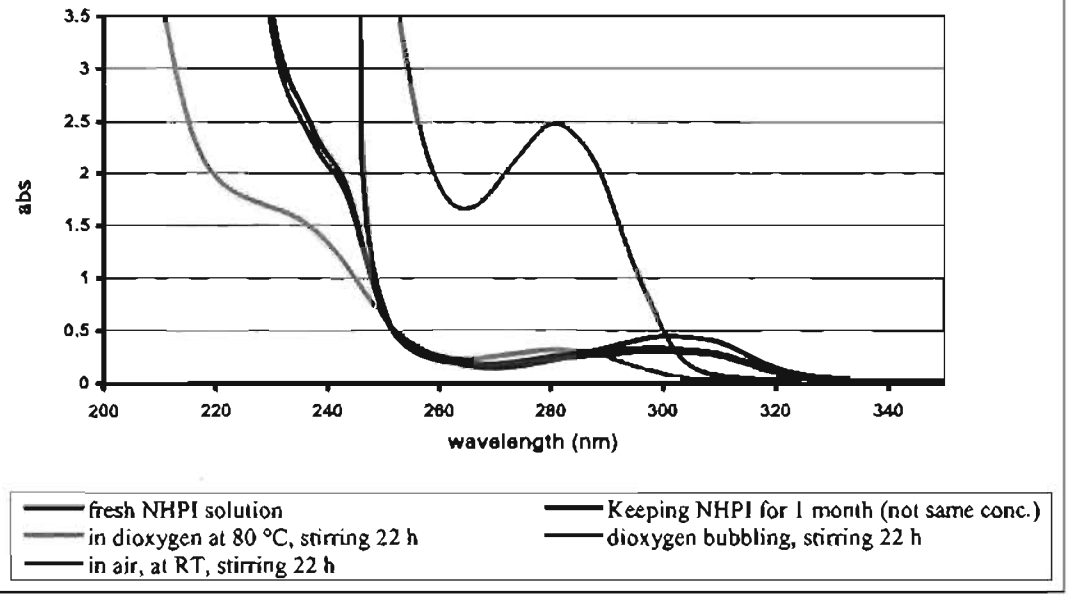


Figure 19: UV-vis spectrum of new complex of cobalt acetate and NHPI at RT vs. 80 °C

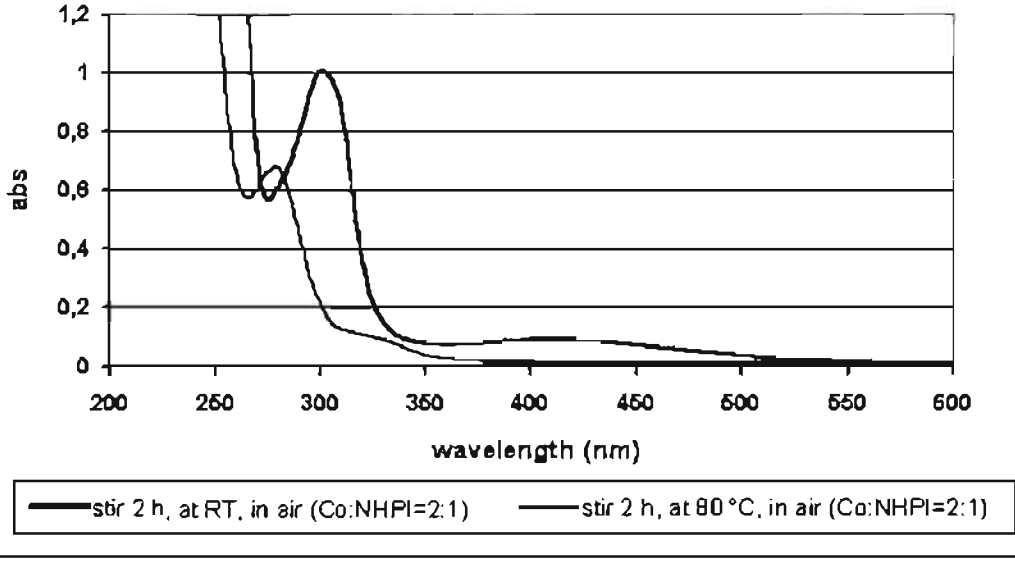
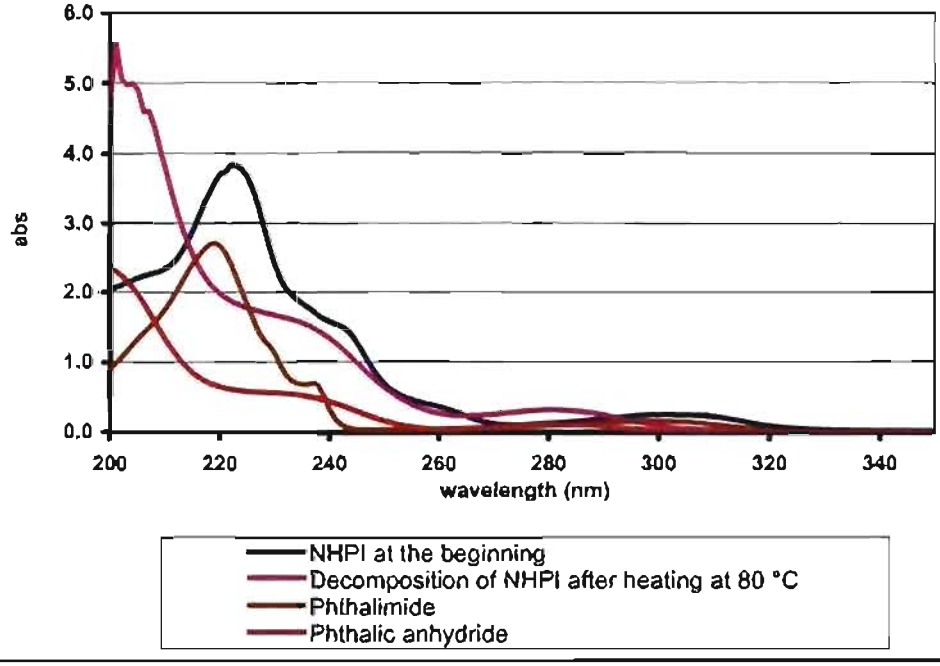


Figure 20: UV-vis spectrum of NHPI, phthalimide, phthalic anhydride, and the decomposition product of NHPI



As we know, high temperature can enhance the effectiveness of NHPI. Although heating also accelerates the decomposition of NHPI in water so as to limit its effectiveness, the combinations of transition metal salts and NHPI still work well and this was already proven in previous work. In these cases, it is believed that the new complex generated from $Co(OAc)_2$ and NHPI plays an important role in this type of radical aerobic oxidations.

4.2 Aerobic oxidations of humic acids

Aerobic oxidations of humic acid sodium salt catalyzed by $Co(OAc)_2$/NHPI/ O_2 were carried out in a 0.003 N NaOH solution at 80 °C in the presence of ben-

zalkonium chloride. Details of experimental work are described in Procedure I on page 58, and the results of these experiments are described below.

Figure 21 shows UV-vis spectra of aqueous humic acid sodium salt solutions at different concentrations. Humic acid absorbs strongly from 200 nm to 400 nm, the absorbance increasing smoothly with decreasing wavelength. Unfortunately, the absorption bands are relatively featureless and provide little information. In some literature reports, a number of UV-vis absorption ratios have been measured, for example the E_4/E_6 ratios (absorbance at 465/665 nm), to provide information about the state of humification and content of humic material.[52] However, the absorption ratios were not helpful to our studies.

Figure 22 compares the UV-vis spectra of the solutions of humic acid sodium salt at the beginning and at the end of the oxidation reactions. As can be seen, the spectra are similar and do not allow any useful conclusion. The absorption bands of the surfactant and NHPI are obscured in these spectra by the very intense absorptions due to a large concentration of humic acids (600 mg). The bands due to NHPI are observed in the spectra for another series of oxidations using less substrate (60 mg, Figure 23). These experiments examined the impact of dilute alkaline media (0.001 N NaOH) on the oxidation of humic acid. Unfortunately, however, no conclusions can be drawn from these experiments because the absorptions due to the substrate did not appear in the spectra. It is, therefore, impossible to conclude whether or to what extent humic acids are oxidized by the catalytic oxidation protocol developed in the present study.

Figure 21: UV-vis spectrum of humic acid sodium salt solutions at different concentrations

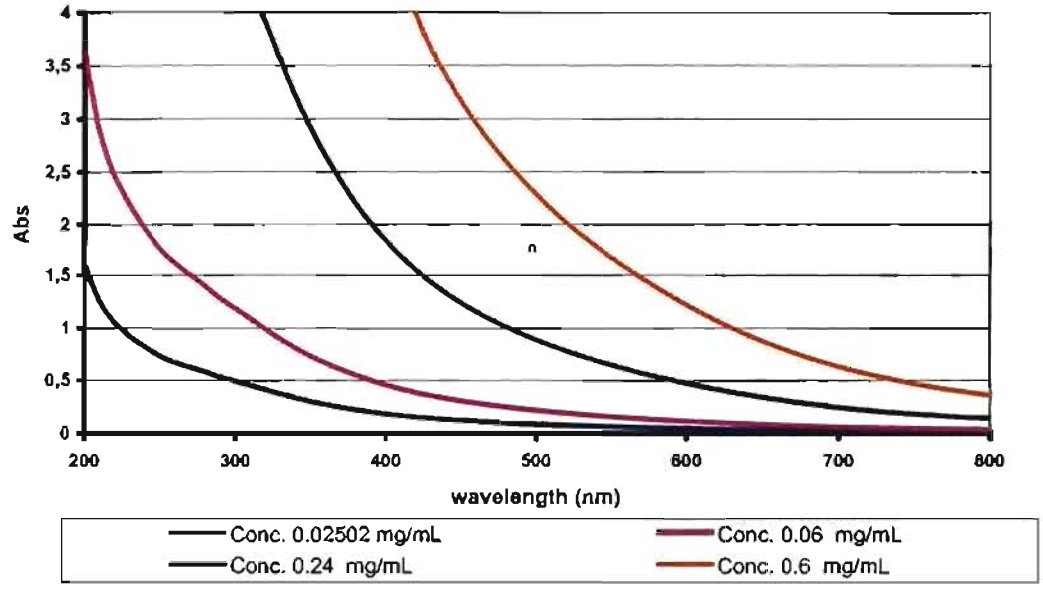


Figure 22: UV-vis spectrum of reaction mixtures of aerobic oxidations of humic acid sodium salts by cobalt acetate / NHPI

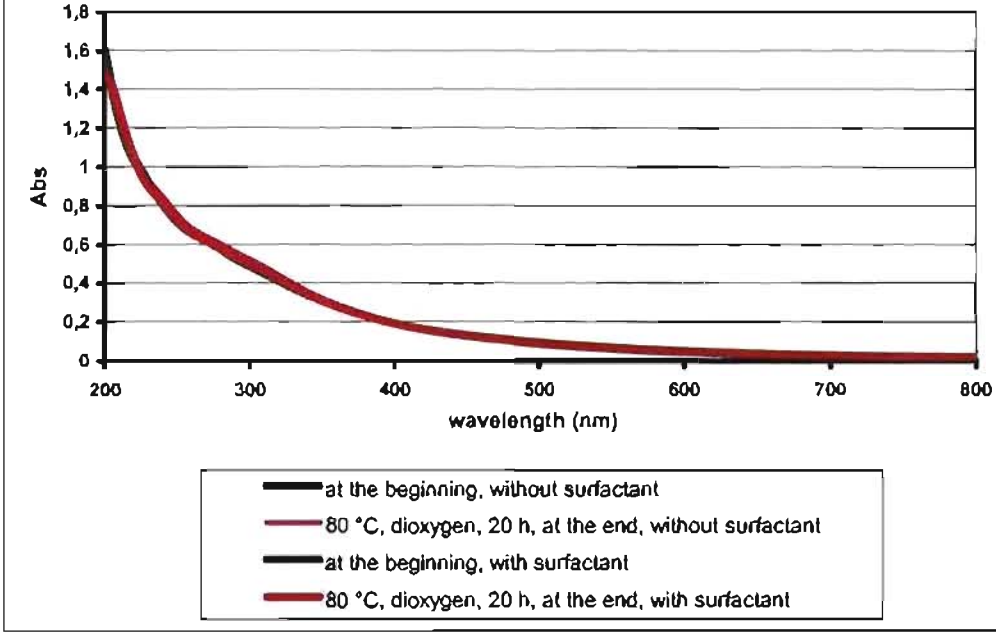
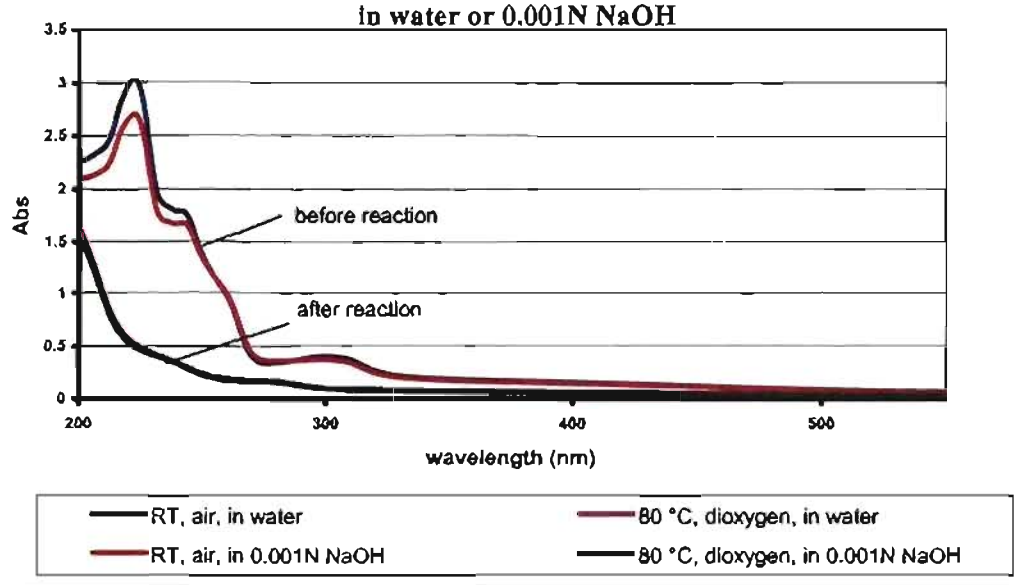


Figure 23: Comparison of UV-vis spectra of oxidations of humic acid sodium salts catalyzed by cobalt acetate / NHPI in water or 0.001N NaOH



4.3 Aerobic oxidations of bauxite

As discussed in Chapter 1, organics in bauxite exist in the form of humic substrates some of which (e.g., humic acids) can be soluble in alkaline solutions. For the purpose of determining how well the organic content of bauxite can be beneficiated by oxidation, it is important to study the solubility of humic substrates as a function of the alkalinity of the reaction medium and the presence of benzalkonium chloride prior to studying the oxidation reactions. Following these studies, we examined the oxidation of bauxite with two different protocols, one using combinations of NHPI and $Co(OAc)_2$ and another using NHPI alone (no added metal catalyst); the latter experiments were undertaken to establish whether iron oxides known to exist in bauxite in significant quantities can promote the aerobic oxidation of the organics. These experiments were analyzed by transferring the

pretreated or oxidized bauxite mixtures into 50-mL centrifuge tubes and diluting to the 40-mL mark with distilled water. Centrifugation afforded a clear upper layer, which was further diluted for UV-vis tests; unless otherwise indicated, 50-fold dilutions were used in general.

4.3.1 Bauxite properties

Visual inspection showed that bauxite solutions changed from colorless to intense yellow with increasing pH; this is also evident from the UV-vis spectra shown in Figure 24 that show absorption bands in the area of 200-450 nm, presumably due to the conjugated macromolecules that are soluble in dilute alkaline solutions (as opposed to iron oxides). The spectra shown in Figures 25 and 26 indicate that the concentration of these organics increases with time, but temperature does not seem to be an important factor in the dissolution process. The spectra in Figure 26 also show that little or no oxidation occurs in the absence of NHPI even at 80 °C; this is in contrast to the known oxidation of organics to oxalate salts in the Bayer process, wherein the solution pH and reaction temperatures are much higher.

Since benzalkonium chloride had a positive influence on the aqueous oxidation of the model substrates, we were interested in studying its impact on dissolving bauxite organics in aqueous media. The results of our experiments indicate that benzalkonium chloride *reduces* the solubility of bauxite (Figure 27).

Figure 24: UV-vis spectra of bauxite in various aqueous conditons after 20-hour stirring at RT in air without catalysts

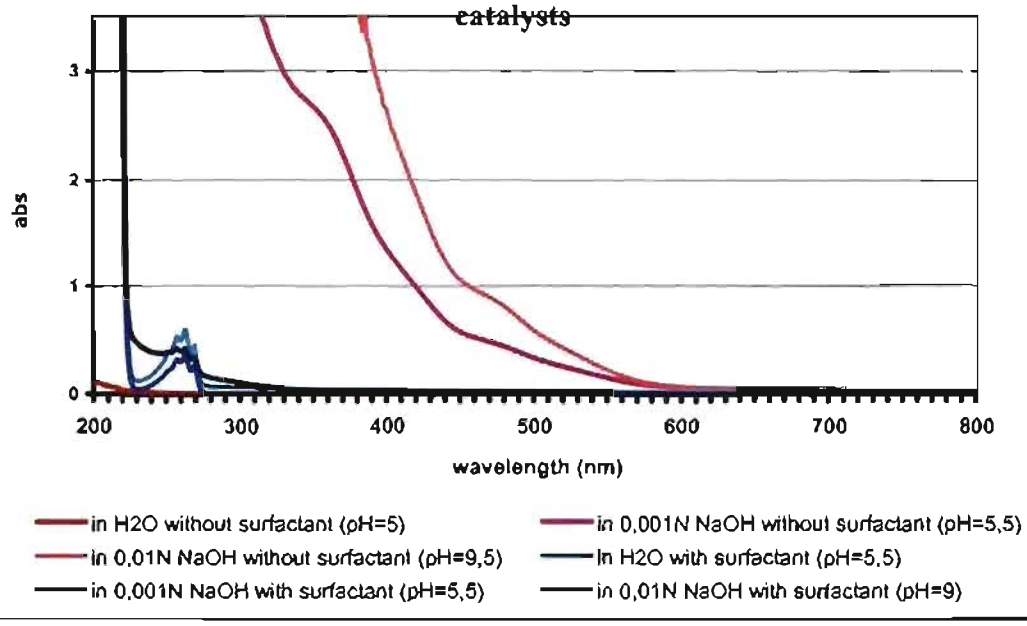


Figure 25: UV-vis spectrum of bauxite stirring in 0.001 N NaOH in air (20-fold dilution; 1-, 10-,and 20 h samplings)

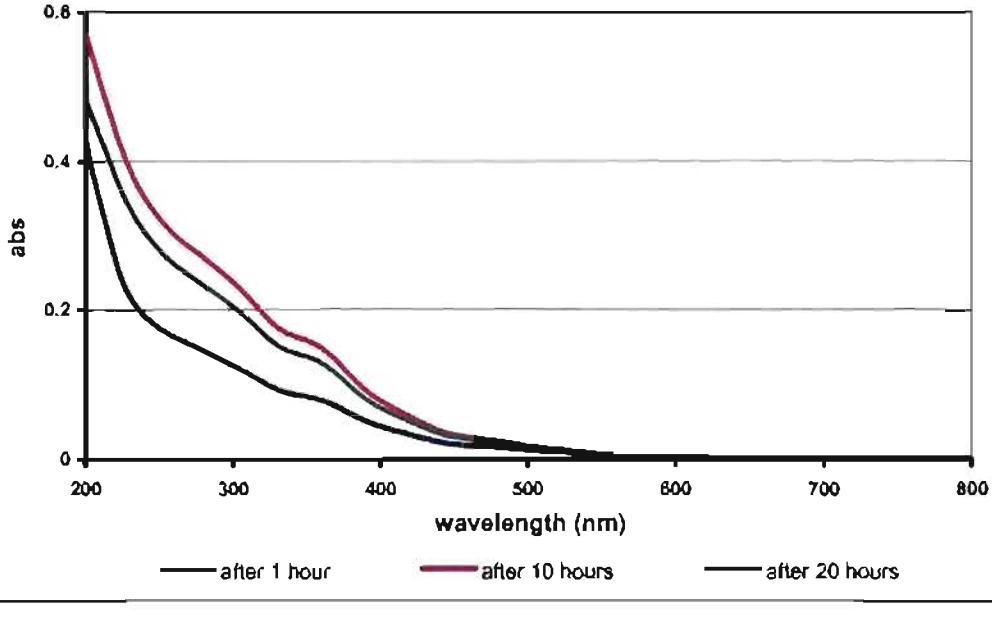


Figure 26: UV-vis spectrum of bauxite in 0.003 N NaOH at different conditions without catalysts

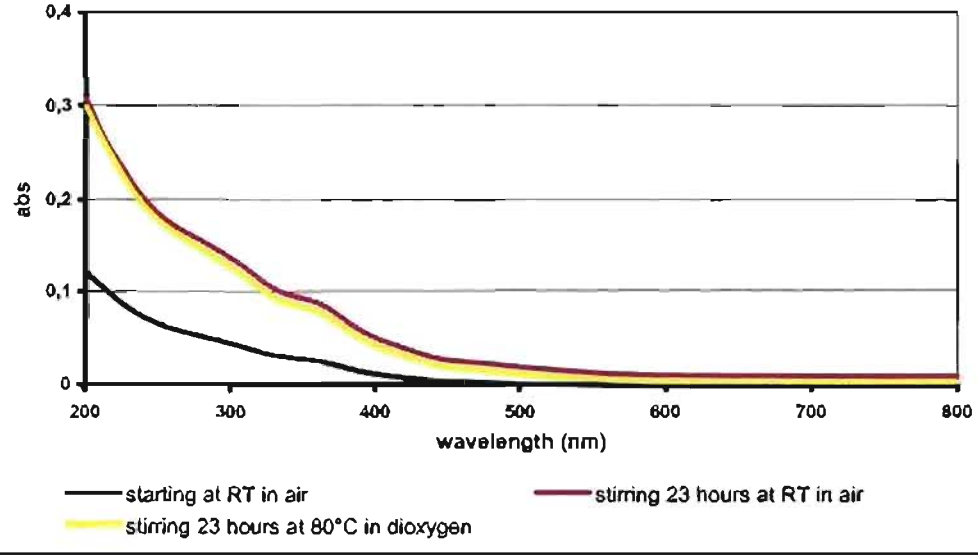
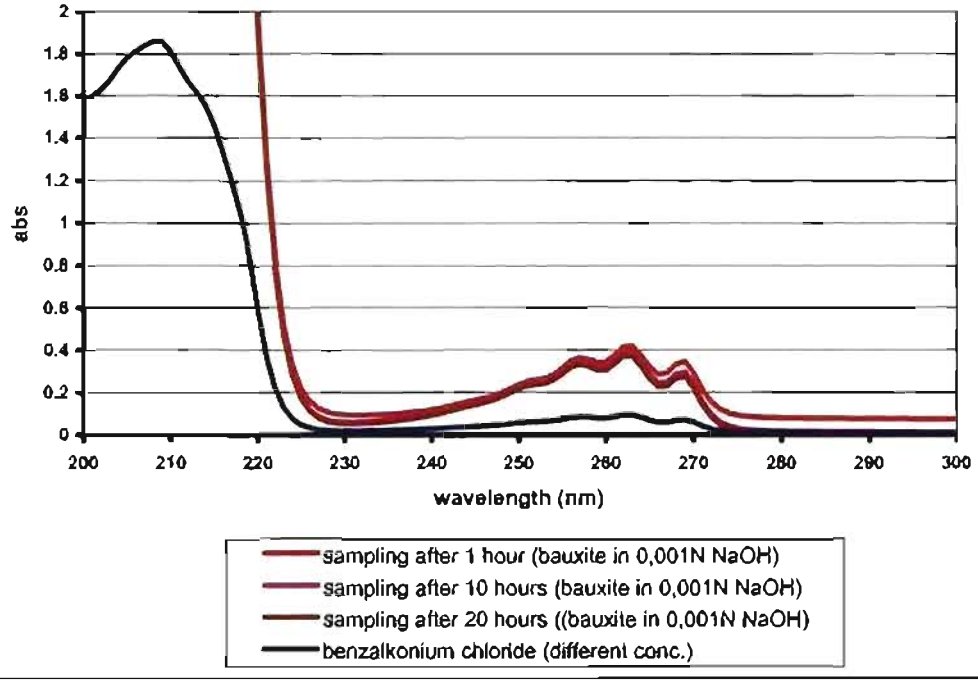


Figure 27: UV-vis spectrum of bauxite in 0.001N NaOH with benzalkonium chloride (sampling at different time)



4.3.2 Bauxite oxidation by NHPI with or without $Co(OAc)_2$

4.3.2.1 Bauxite oxidation catalyzed by $Co(OAc)_2$/NHPI

We have studied the effectiveness of NHPI/$Co(OAc)_2$ in aerobic oxidations of bauxite in dilute alkaline solutions. As mentioned earlier, the alkalinity of the reaction medium can have an important impact on the amount of organics dissolving in bauxite mixtures. In this respect, the bauxite samples were subjected to a pretreatment step consisting of stirring in a 0.003N NaOH solution for 20 h in air at RT prior to the oxidation reaction. It was hoped that this approach would counteract the effect of introducing acidic NHPI into the reaction mixture.

Figures 28 and 29 show UV-vis spectra of the reaction mixtures obtained from the aerobic oxidations of bauxite under different conditions. Inspection of the spectra in Figure 28 shows little or no difference between the reaction mixtures obtained from high-temperature oxidations (the red trace for aerobic oxidation of bauxite without pretreatment and the pink one for oxidation of bauxite after pretreatment), and also indicates that NHPI (absorption band at 300 nm) decomposes to phthalic anhydride (absorption band at 280 nm) in the oxidation reactions. The spectra in Figure 29 shows the UV-vis spectra of the bauxite sample after pretreatment but prior to the oxidation reaction (amber trace) and the spectra of the mixtures obtained from the oxidation of samples with (pink trace) and without (blue trace) pretreatment; it should be noted that the absorptions due to the NHPI/$Co(OAc)_2$ system have been subtracted from the latter spectra in order to simplify the comparison. Comparing the UV-vis spectra of post-oxidation mixtures (pink and blue traces) to that of the pre-treated sample prior to oxidation

(amber trace) indicates that some of the organics present in the mixture were oxidized by the catalytic system. Visual inspection of the samples also showed that oxidation turns the sample color from the initial muddy brown to a lighter shade, consistent with the decrease in the intensity of the absorption peaks observed in the spectra. It should be emphasized, however, that the insoluble portion of the bauxite sample was not removed from the reaction mixture, which might result in a continual dissolution of organics into the sample and hence no dramatic color change would be expected.

Figure 28: Comparison of UV-vis spectra of bauxite oxidations catalyzed by cobalt acetate and NHPI

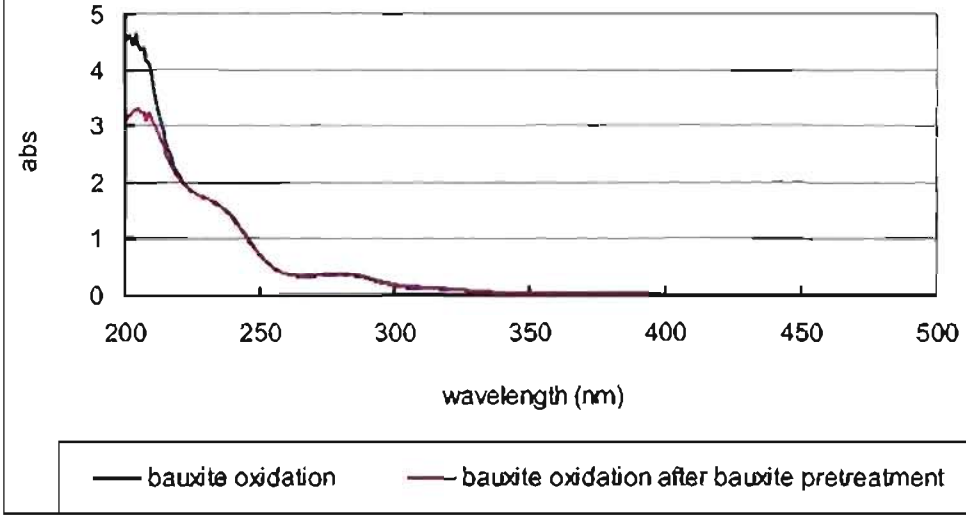
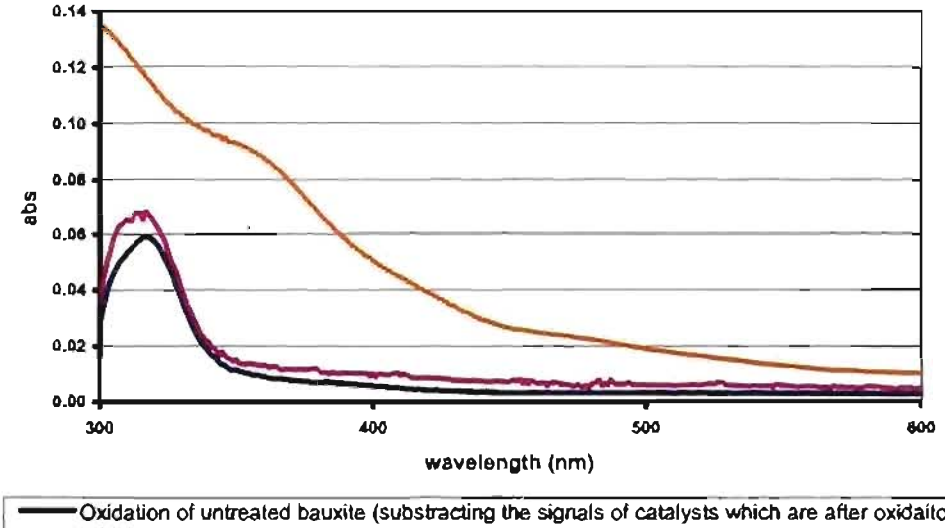


Figure 29: UV-vis spectrum of bauxite oxidations catalyzed by cobalt acetate / NHPI with or without pretreatment



4.3.2.2 Bauxite oxidation by NHPI without cobalt acetate

Figure 30 shows the UV-vis spectra obtained from the experiments conducted on bauxite samples containing added NHPI only (no $Co(OAc)_2$). The absorption band due to NHPI is present at the beginning of bauxite oxidation (blue trace), but it disappears because NHPI decomposes after aerobic oxidation at 80 °C for 20 h (pink trace). Figure 31 compares the UV-vis spectra of bauxite samples before (blue trace) and after (pink and red traces) oxidation with NHPI. Inspecting the spectra region not obscured by NHPI absorptions (350-450 nm) showed that showed that the dissolved organics were oxidized by NHPI. Figure 32 shows the same spectra after subtracting the absorptions due to NHPI further confirm that dissolved organics have been oxidized.

Figure 30: Comparison of UV-vis spectra between at the beginning and at the end of bauxite oxidation catalyzed by NHPI alone

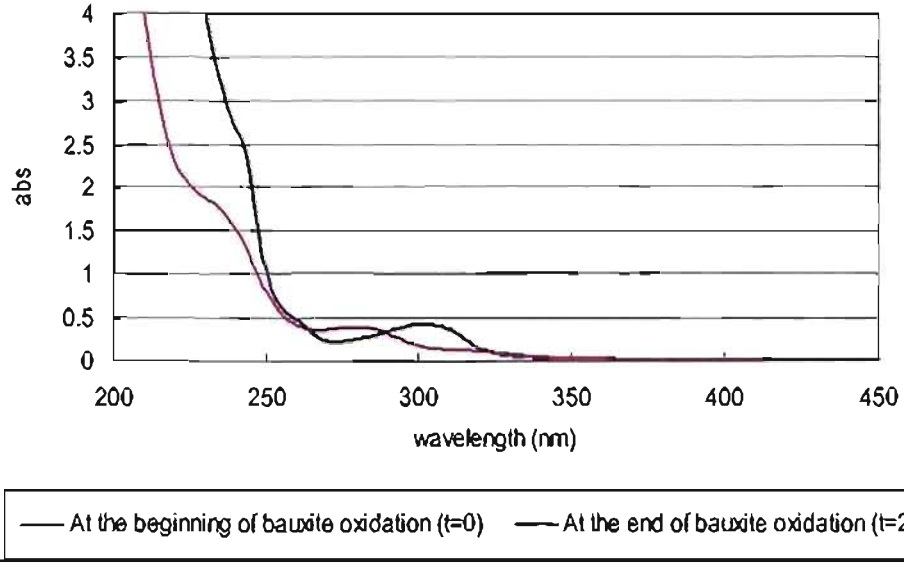


Figure 31: Comparison of UV-vis spectra of bauxite oxidations catalyzed by NHPI

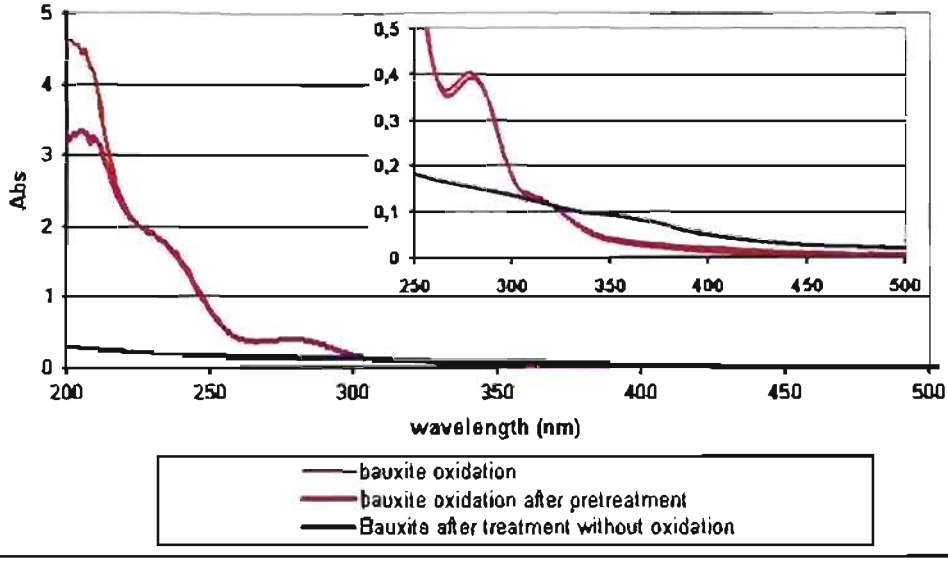
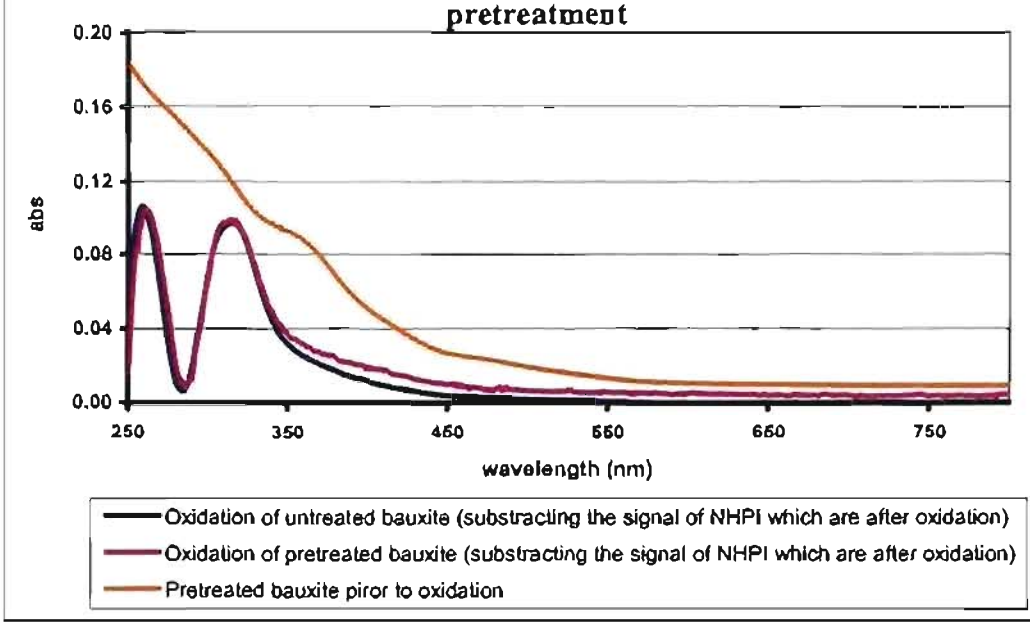


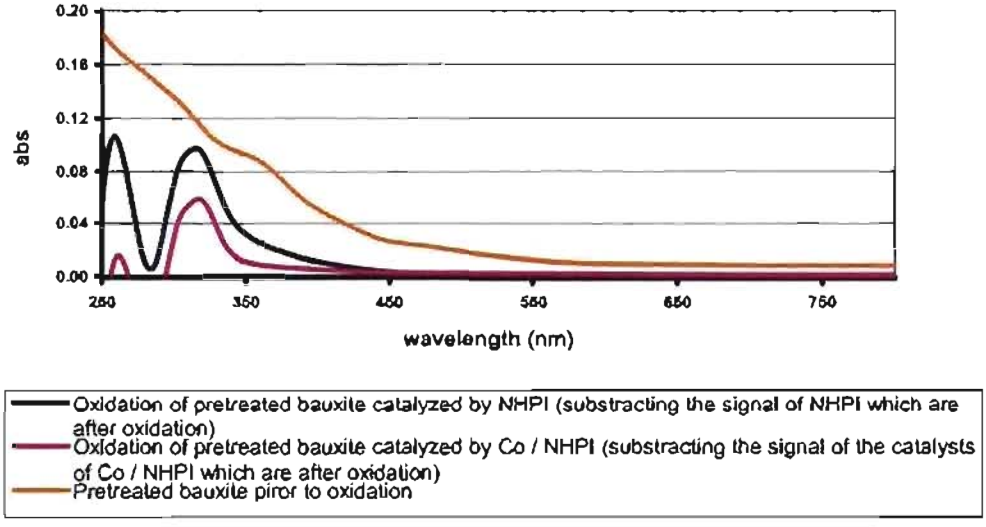
Figure 32: Comparison of UV-vis spectrum of bauxite oxidations catalyzed by NHPI with and without pretreatment



4.3.2.3 Bauxite oxidation by $Co(OAc)_2$ / NHPI

Figure 33 shows the UV-vis spectra of mixtures obtained from aerobic oxidations of pretreated bauxite catalyzed by NHPI alone and by $Co(OAc)_2$ / NHPI. It can be seen that both systems are effective in the oxidation of dissolved organics, and although the $Co(OAc)_2$ / NHPI system appears to be somewhat more effective, it is difficult to ascertain how significant this difference is.

Figure 33: Comparison of UV-vis spectra of aerobic oxidations of pretreated bauxite catalyzed by NHPI alone or cobalt acetate / NHPI



4.3.3 Conclusions on bauxite oxidations

In our studies of bauxite oxidations, we met some problems in analysis. We cannot qualify and quantify organics in bauxite solids and solutions. UV-vis spectrometer can give us some help, but not the best. However, at least, we can make sure one point from the above results: NHPI can works for bauxite oxidations in alkaline solutions, even without the help of cobalt acetate.

Chapter 5: GLOBAL CONCLUSIONS

The studies conducted during this M. Sc. project have shown that NHPI is a highly effective co-catalyst for metal-catalyzed aerobic oxidation of organic substances. The most extensively investigated metal salt for catalytic oxidations described in this thesis is $Co(OAc)_2$, but a number of simple iron salts were also examined in certain cases. Literature reports have indicated that combinations of NHPI and iron salts such as $Fe(acac)_3$ provide less efficient catalytic activities compared to NHPI/$Co(OAc)_2$ systems.[38] Our studies have also confirmed that much higher loadings of iron salts are required for obtaining oxidation activities comparable to those obtained with $Co(OAc)_2$. However, we have shown that much less expensive sources of iron can be employed for these reactions (e.g., Fe_2O_3 or $Fe(NO_3)_3$), making higher catalyst loadings less onerous from an economical point of view. In addition, since bauxite samples are known to contain fairly large concentrations of iron oxides (ca. 15%), the use of this metal is very advantageous for our purposes. Thus, our preliminary results indicate that aerobic oxidation of bauxite is facilitated by the addition of NHPI only, no added metal salts being necessary.

Another important finding of our studies is that aerobic oxidations can be carried out in aqueous media. Thus, our results indicate that iron salts, and especially $Fe(NO_3)_3$, are more active in aqueous media than $Co(OAc)_2$. Significantly, the use of phase transfer catalysts or surfactants does not seem to be necessary. The catalytic efficacy of the $Fe(NO_3)_3$/NHPI system is also less sensitive to the variations

of solution alkalinity. These findings are significant for the objective of developing a practical protocol for bauxite beneficiation, because relying on iron salts that are present in bauxite and doing the oxidation reactions in inexpensive and environmentally friendly aqueous media would render such a protocol commercially viable.

One remaining challenge in our studies is the requirement for high temperatures (80 °C) in the oxidation reactions. The need for heating is not only disadvantageous from a cost-benefit analysis, but also detrimental for the longevity of the catalytic system since our studies showed that NHPI is thermally unstable in aqueous media, decomposing over 2 hours at 80 °C to give phthalic anhydride. Therefore, an acceptable oxidation protocol should ultimately operate at lower temperatures to avoid this decomposition and improve the economical viability of the overall process.

Over the short term, an even more important practical problem is related to the quantification of bauxite oxidation reactions. Our studies showed that UV-visible absorption spectra offer a rough estimate of how much organic matter has been destroyed as a result of oxidation, but this measure is indirect and not very quantitative. We have also tested the possibility of using combustion analysis but the results to date are not very encouraging. It is hoped that during the next phase of this project efforts will be directed at studying the feasibility of using techniques such as Chemical Oxidation Demand (COD) and Total Organic Carbon (TOC) for quantifying the oxidation of bauxite samples. Another important and potentially effective parameter to study would be the impact of light (UV or sunlight) on the oxidation efficacy. It is postulated that light can enhance the generation and reac-

tivities of radical species known to be involved in these oxidation processes; it should be added, however, that sources of light other than sunlight are quite inexpensive for most applications.

REFERENCES

[1] G. Lever, Internal Alcan report (no. A-RC-468-76-3590), ***1976.***

[2] K. The, Internal Alcan report (no. AR-98/0014), April ***1998.***

[3] To be sure, the oxidation of lignin and humic acids with CuO / NaOH, $KMnO_4$, or peracetic acid has been carried out for the purposes of identifying the degradation products.

[4] A) M. Schnitzer, ***1965.*** **The application of infrared spectroscopy to investigations on soil humic compounds**. *Can. J. Spectrosc., 10*: 121-127.

B) D. S. Gamble, ***1970.*** **Titration curves of fulvic acid: the analytical chemistry of a weak acid polyelectrolyte.** *Can. J. Chem., 48 (20)*: 3197-3204

C) D. S. Gamble, ***1972.*** **Potentiometric titration of fulvic acid: equivalence point calculations and acidic functional gruops.** *Can. J. Chem., 50 (16)*: 2680-2690.

D) M. Schnitzer and S. U. Khan, ***1972.*** **Humic Substances in the Environment**. Marcel Dekker, New York, 327 pp.

E) M. Schnitzer and S. U. Khan, ***1978.*** **Soil Organic Matter**. Elsevier, Amsterdam.

F) P. Ruggiero, F. S. Interesse, L. Cassidei, and O. Sciacovelli, ***1980.*** **^{1}H NMR spectra of humic and fulvic acids and their peracetic oxidation products.** *Geochim. Cosmochim. Acta. 44:* 603-609.

G) J. R. Eterl, and J. I. Hedges, ***1983.*** **Chemical and spectroscopic properties of marine and terrestrial humic acids, melanoidines, and catechol-based synthetic polymers.** In: R. Christman and E. Gjessing (Editors),

Aquatic and Terrestrial Humic Materials. Ann Arbor Sci., Ann Arbor, Michigan, pp. 143-163.

H) P. G. Hatcher, I. A. Breger, L. W. Dennis, and G. E. Maciel, ***1983***. **Solid-state ^{13}C NMR of sedimentary humic substances: new-revelations on their chemical composition**. In: R.F. Christman and E.T. Gjessing (Editors), Aquatic and Terrestrial Humic Materials. Ann Arbor Sci., Ann Arbor, Michigan, pp. 37-81.

I) P. G. Hatcher, M. Schnitzer, A. M. Vassallo, and M. A. Wilson, ***1989***. **The chemical structure of highly aromatic humic acids in three volcanic ash soils as determined by dipolar dephasing NMR studies**. *Geochim. Cosmochim. Acta, 53:* 125-130.

J) G. R. Aiken, D. M. McKnight, R. L. Wershaw, and P. M. McCarthy, ***1985***. **An introduction into humic substances in soil, sediment, and water**. In: G.R. Aiken, D.M. McKnight, R.L. Wershaw and P.M. McCarthy (Editors), Humic Substances in Soil, Sediment, and Water. Wiley-Interscience, New York, NY, pp. 1-9.

K) P. MacCarthy, S. J. DeLuca, K. J. Voorhees, R. L. Malcolm, and E. M. Thurman, ***1985***. **Pyrolysis-mass spectrometry/pattern recognition on a well characterized suite of humic samples.** *Geochim. Cosmochim. Acta, 49:* 2091-2096.

L) K. Pihlaja, J. Peuravuori, P. Vainiotalo, B. Nordén, ***1990***. **Some aspects of the characterization of humic substances in lake waters.** In: B. Allard, H. Boren and A. Grimvall (Editors), Humic Substances in the Aquatic and Terrestrial Environment. Lecture Notes in Earth Sciences, Vol. 33. Springer-Verlag, New York, NY, pp. 113-121.

M) J. Peuravuori and K. Pihlaja, ***1990***. **Isolation and fractionation of humic substances in lake waters.** In: B. Allard, H. Boren and A. Grimvall (Editors), Humic Substances in the Aquatic and Terrestrial Environment. Lecture

Notes in Earth Sciences, Vol. 33. Springer-Verlag, New York, NY, pp. 123-134.

N) A. Singer and P. M. Huang, ***1990.*** **Nature of humic substances of mollisol and luvisol in the Canadian Prairies.** In: B. Allard, H. Boren and A. Grimvall (Editors), Humic Substances in the Aquatic and Terrestrial Environment. Lecture Notes in Earth Sciences, Vol. 33. Springer-Verlag, New York, NY, pp. 151-161.

O) F. Y. Saleh, W. A. Ong, I. Kim, and Q. Haj-Mahmoud, ***1990.*** **Structural features of aquatic fulvic acids by analytical and preparative HPLC followed by spectroscopic characterization.** In: B. Allard, H. Boren and A. Grimvall (Editors), Humic Substances in the Aquatic and Terrestrial Environment. Lecture Notes in Earth Sciences, Vol. 33. Springer-Verlag, New York, NY, pp. 47-61.

P) N. Senesi, T. M. Miano, and M. R. Provenzano, ***1990.*** **Fluorescence spectroscopy as a means of distinguishing fulvic acid and humic acids from dissolved and sedimentary aquatic sources and terrestrial sources.** In: B. Allard, H. Boren and A. Grimvall (Editors), Humic Substances in the Aquatic and Terrestrial Environment. Lecture Notes in Earth Sciences, Vol. 33. Springer-Verlag, New York, NY, pp. 63-73.

Q) S. A. Wood, ***1996.*** **The role of humic substances in the transport and fixation of metals of economic interest (Au, Pt, Pd, U, V).** *Ore Geology Reviews 11:* 1-31

[5] H. R. Schulten and M. Schnitzer, ***1993.*** **A state of the art structural concept for humic substances.** *Naturwissenschaften 80:* 29.

[6] R. A. Sheldon and H. van Bekkum. ***2000.*** **Fine Chemicals through Heterogeneous Catalysts.** WILEY-VCH, New York, Chapter 9, pp.473-549.

[7] K. Kaneda, T. Itoh, N. Kii, K. Jitsukawa, and S. Teranishi, ***1982.*** **Oxygenation of enamines using copper catalyst.** *J. Mol. Catal. 15:* 349-365.

[8] M. Tokunaga, Y. Shirogane, H. Aoyama, Y. Obora, and Y. Tsuji, ***2005.*** **Copper-catalyzed oxidative cleavage of carbon-carbon double bond of enol ethers with molecular oxygen.** *J. Org. Chem. 690:*5378-5382.

[9] F. Wang, G. Y. Yang, W. Zhang, W. H. Wu, and J. Xu, ***2003.*** **Copper and manganese: two concordant partners in the catalytic oxidation of p-cresol to p-hydroxybenzaldehyde.** *Chem. Comm.*, 1172-1173.

[10] N. Komiya, T. Naota, and S. I. Murahashi, ***1996.*** **Aerobic oxidationof alkanes in the presence of acetaldehyde catalysed by copper-crown ether.** *Tet. Lett., Vol. 37, No. 10:* 1633-1636.

[11] N. Komiya, T. Naota, Y. Oda, and S. I. Murahashi, ***1997.*** **Aerobic oxidation of alkanes and alkenes in the presence of aldehydes catalyzed by copper salts and copper – crown ether.** *J. Mol. Catal. A: Chem. 117:* **21-37.**

[12] I. E. Markó, A. Gautier, J. L. Mutonkole, and R. Dumeunier, ***2001.*** **Neutral, non-racemising, catalytic aerobic oxidation of alcohols.** *J. Organomet. Chem. 624:* 344-347.

[13] I. E. Markó, A. Gautier, R. Dumeunier, K. Doda, F. Philippart, S. M. Brown, and C. J. Urch, ***2004.*** **Efficient, copper-catalyzed, aerobic oxidation of primary alcohols.** *Angew. Chem. Int. Ed. 43:* 1588-1591.

[14] S. I. Murahashi, Y. Oda, and T. Naota, ***1992.*** **Iron-and Ruthenium-catalyzed oxidations of alkanes with molecular oxygen in the presence of aldehydes and acids.** *J. Am. Chem. Soc. 114:* 7913-7914.

[15] N. Perkas, Y. Wang, Y. Kotypin, A. Gedanken, and S. Chandrasekaran, ***2001***. **Mesoporous iron-titania catalyst for cyclohexane oxidation.** *Chem. Comm.* 988-989.

[16] S. I. Murahashi, X. G. Zhou, and N. Komiya, ***2003***. **Chlorinated phthalocyanine iron(II) complex catalyzed oxidation of alkanes and alkenes with molecular oxygen in the presence of acetaldehyde**. *Synlett, No.3:* 321-324

[17] D. H. Barton, T. S. Li, and J. MacKinnon, ***1997***. **Synergistic oxidation of cyclohexane and hydrogen under Gif conditions.** *Chem. Comm.* 557-558.

[18] Z. Wang, A. E. Martell, and R. J. Motekaitis, ***1998***. **Hydroxylation of alkanes by molecular oxygen with dinuclear Fe(II) macrocyclic complexes as catalysts.** *Chem. Comm.,* 1523-1524.

[19] J. E. Lyons, P. E. Ellis, Jr., H. K. Myers, Jr., ***1995***. **Halogenated metalloporphyrin complexes as catalysts for selective reactions of acyclic alkanes with molecular oxygen.** *J. Catal. 155:* 59-73.

[20] S. Evans and J. R. L. Smiths, ***2000***. **The oxidation of ethylbenzen and other alkylaromatics by dioxygen catalysed by iron(III) tetrakis-(pentafluorophenyl)porphyrin and related iron porphyrins.** *J. Chem. Soc., Perkin Trans. 2,* 1541-1551.

[21] A. Maldotti, C. Bartocci, G. Varani, A. Molinari, and D. Mansuy, ***1996***. **Oxidation of cyclohexane by molecular oxygen photoassisted by meso-tetraarylporphyrin iron(III)-hydroxo complexes.** *Inorg. Chem. 35,* 1126-1131.

[22] C. Nozaki, M. Misono, N. Mizuno, ***1998***. **Oxidation of cyclohexane with molecular oxygen efficiently catalyzed by di-iron(III)-substituted sillicotung-**

state, γ-$SiW_{10}\{Fe(OH)_2\}_2O_{38}^{6-}$, including radical-chain mechanism. *Chem. Lett.* 1263-1264.

[23] N. Mizuno, M. Tateishi, T. Hirose, and M. Iwamoto, ***1993.*** **Oxygenation of alkanes by molecular oxygen on $[PW_9O_{37}\{Fe_2Ni(OAc)_3\}]^{10-}$ heteropolyanion.** *Chem. Lett.* 2137-2140.

[24] T. Iwahama, K. Syojyo, S. Sakaguchi, and Y. Ishii, ***1998.*** **Direct Conversion of cyclohexane into adipic acid with molecular oxygen catalyzed by N-hydroxyphthalimide combined with $Mn(acac)_2$ and $Co(OAc)_2$.** *Org. Proc. Res. Dev., 2*: 255-260.

[25] S. A. Chavan, D. Srinivas, and P. Ratnasamy, ***2001.*** **A novel, zeolite-encapsulated μ_3-oxo Co/Mn cluster catalyst for oxidation of *para*- xylene to terephthalic acid.** *Chem. Comm.*, 1124-1125.

[26] R. S. Drago and A. S. Goldstein, ***1991.*** **Oxidation of alkanes by Cobalt(II) salts of weakly coordinating anions.** *Inorg. Chem. 30:* 4506-4510.

[27] T. Punniyamurthy, S. J. S. Kalra, and J. Iqbal, ***1995.*** **Cobalt(II) catalyzed biomimetic oxidation of hydrocarbons in the presence of dioxygen and 2-methylpropanal.** *Tet. Lett., Vol. 36, No. 46:* 8497-8500.

[28] S. I. Murahashi, T. Naota, and N. Komiya, ***1995.*** **Metalloporphyrin-catalyzed oxidation of alkanes with molecular oxygen in the presence of acetaldehyde.** *Tet. Lett., Vol 36, No. 44:* 8059-8062.

[29] D. E. Hamilton, R. S. Drago, and A. Zombeck, ***1987.*** **Mechanistic studies on the cobalt Schiff base catalyzed oxidation of olefins by O_2.** *J. Am. Chem. Soc. 109:* 374-379.

[30] J. Y. Qi, H. X. Ma, X. J. Li, Z. Y. Zhou, M. C. K. Choi, A. S. C. Chan, and Q. Y. Yang, ***2003.*** **Synthesis and characterization of cobalt(III) complexes containing 2-pyridinecarboxamide ligands and their application in catalytic oxidation of ethylbenzene with dioxygen.** *Chem. Comm.* 1294-1295.

[31] K. Nair, D. P. Sawant, G. V. Shanbhag, and S. B. halligudi, ***2004.*** **Aerial oxidation of substituted aromatic hydrocarbons catalyzed by Co/Mn/Br^- in water-dioxane medium.** *Catal. Commun. 5*: 9-13.

[32] E. Grochowski, T. BolesŁawska, and J. Jurczak, ***1977.*** **Reaction of diethyl azodicarboxylate with ethers in the presence of N-Hydroxyimides as catalysts.** *Synthesis*, 718-720

[33] J. Foricher, C. Fübringer, K. Pfoertner, (Hoffmann La Roche), ***1986.*** **Catalytic allylic oxidation of isoprenoids with N-hydroxy dicarboxylic acid imides.** *Eur. Pat.* 198,351

[34] Y. Ishii and S. Sakaguchi, ***1999.*** **A new strategy for alkane oxidation with dioxygen using N-hydrophthalimide as a radical catalyst.** *Catal. Surveys Japan, 3,* 27-35.

[35] Y. Yoshino, Y. Hayashi, T. Iwahama, S. Sakaguchi, and Y. Ishii, ***1997.*** **Catalytic oxidation of alkylbenzenes with molecular oxygen under normal pressure and temperature by N-hydroxyphthalimide combined with $Co(OAc)_2$.** *J. Org. Chem. 62,* 6810-6813.

[36] Y. Ishii, T. Iwahama, S. Sakaguchi, K. Nakayama, and Y. Nishiyama, ***1996.*** **Alkane oxidation with molecular oxygen using a new efficient catalytic system: N-hydroxyphthalimide combined with Co(acac)n (n=2 or 3).** *J. Org. Chem. 61,* 4520.

[37] T. Iwahama, Y. Yoshino, T. Keitoku, S. Sakaguchi, and Y. Ishii, ***2000.*** **Efficient Oxidation of Alcohols to Carbonyl Compounds with molecular oxygen catalyzed by N-Hydroxyphthalimde Combined with a Co Species,** *J. Org. Chem., 65,* 6502-6507.

[38] A. Shibamoto, , S. Sakaguchi, and Y. Ishii, ***2000.*** **Aerobic Oxidation of Methylpyridines to Pyridinecarboxylic Acids Catalyzed by N-Hydroxyphthalimide,** *Org. Proc. Res. Dev., 4,* 505-508

[39] A) Y. Kamiya, T. Nakajima, and K. Sakoda, ***1966.*** **Autoxidation of p-xylene catalyzed with cobalt monobromide in acetic acid.** *Bull. Chem. Soc. Jpn., 39,* 2211-2215.

B) Y. Kamiya and M. Kotake, ***1973.*** **Catalysis of manganese salts in the autoxidation of cyclohexanone.** *Bull. Chem. Soc. Jpn., 46,* 2780-2784.

[40] F. Rajabi and B. Karimi, ***2005.*** **Efficient aerobic oxidation of alcohols using a novel combination N-Hydroxy phthalimide and a recyclable heterogeneous complex,** *J. Mol. Catal. A: Chem., 232,* 95-99.

[41] Y. Ishii, S. Sakaguchi, and T. Iwahama, ***2001.*** In page 405 of **"Innovation of hydrocarbon oxidation with molecular oxygen and related reactions".** *Adv. Synth. Catal. 343, No.5,* 395-427.

[42] Y. Tashiro, T. Iwahama, S. Sakaguchi, and Y. Ishii, ***2001.*** **A new strategy for the preparation of terephthalic acid by the aerobic oxidation of p-xylene using N-hydroxyphthalimide as a catalyst.** *Adv. Synth. Catal., 343, No. 2,* 220-225.

[43] B. B. Wenzel, M. P. J. Donners, P. L. Alsters, M. C. Feiters, and R. J. M. Nolte, ***2000.*** **NHPI / Co(II) catalyzed low temperature Benzylic Oxidation using Molecular Oxygen,** *Tetrahedron 56,* 7797-4803

[44] C. Annunziatini, M. F. Gerini, O. Lanzalunga, and M. Lucarini, ***2004.*** **Aerobic oxidation of benzyl alcohols catalyzed by aryl substituted N-hydroxy-phthalimides. Possible involvement of a charge–transfer complex.** *J. Org. Chem. 69,* 3431-3438.

[45] C. Annunziatini, P. Baiocco, M. F. Gerini, O. Lanzalunga, and B. SjÖgern, ***2005.*** **Aryl substituted N-hydroxyphthalimides as mediators in the lac-case- catalysed oxidation of lignin model compounds and delignification of wood pulp,** *J. Mol. Catal. B: Enz. 32,* 89-96.

[46] N. Hirai, N. Sawatari, N. Nakamura, S. Sakaguchi, and Y. Ishii, ***2003.*** **Oxidation of Substituted Toluenes with Molecular Oxygen in the presence of N, N', N"-Trihydroxy-isocyanuric Acid (THICA) as a key Catalyst,** *J. Org. Chem., 68,* 6587-6590.

[47] S. Mukhopadhyay and S. B. Chandalia, ***1999.*** **Kinetics and process parameter studies in highly selective air oxidation of side-chain alkyl groups in picolines, 2-methylnappthalene, and pseudocumene.** *Org. Proc. Res. Dev. 3,* 227-331.

[48] C. Einhorn, J. Einhorn, C. Marcadal, and J. L. Pierre. ***1997.*** **Oxidation of organic substrates by molecular oxygen mediated by N-hydroxyphthalimide (NHPI) and acetaldehyde,** *Chem. Comm.,* 447-448.

[49] C. Einborn, J. Einborn, and C. Marcadal-Abbadi, ***2001.*** **"Mild and convenient one pot synthesis of N-Hydroxyimides from N-unsubstituted imides."** *Synth. Commun. 32 (5),* 741-748.

[50] K. Sugamoto, Y. Matsushita, Y. Kameda, M. Suzuki, and T. Matsui. ***2005***. "**Microwave-assisted synthesis of N-Hydroxy-phthalimide Derivates.**" *Synth. Commun. 35:* 67-70.

[51] N. Hirai, T. Kagayama, Y. Tatsukawa, S. Sakaguchi, and Y. Ishii. ***2004***. "**Development of an efficient method for preparation of 1,3,5-trihydroxyisocyanuric acid (THICA) and its use as aerobic oxidation catalyst.**" *Tet. Lett. 45:* 8277-8280.

[52] F. J. Stevenson. ***1994***. **Humus chemistry: Genesis, Composition, Reactions,** 2nd Ed., John Wiley & Sons Inc.